# CLINICOPATHOLOGICAL ANALYSIS OF OVARIAN TUMORS AND THE ROLE OF p53 AND Ki- 67 IN SURFACE EPITHELIAL TUMORS OF OVARY

**DISSERTATION**

**SUBMITTED FOR M.D(PATHOLOGY)**

**BRANCH III**

**APRIL – 2013**


**THE TAMILNADU DR. M.G.R. MEDICAL UNIVERSITY**
**CHENNAI – TAMILNADU**

# CERTIFICATE

This is to certify that this dissertation titled **"CLINICOPATHOLOGICAL ANANLYSIS OF OVARIAN TUMORS AND THE ROLE OF p53 AND Ki-67 IN SURFACE EPITHELIAL TUMORS OF OVARY"** is the original and bonafide work done by **Dr.G.Gayathiri** under the guidance of **Dr.N.ARUMUGAM, M.D**., Professor&Head, Department of pathology at the Thanjavur medical college and Hospital, Thanjavur, during the tenure of her course in M.D. Pathology from May-10 to April 13 held under the regulation of the Tamilnadu Dr.M.G.R. Medical University,Guindy, Chennai- 600032.

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**Place: Thanjavur** **Place: Thanjavur**

**Date: .12. 2012** **Date: .12.2012**

## CERTIFICATE BY THE GUIDE

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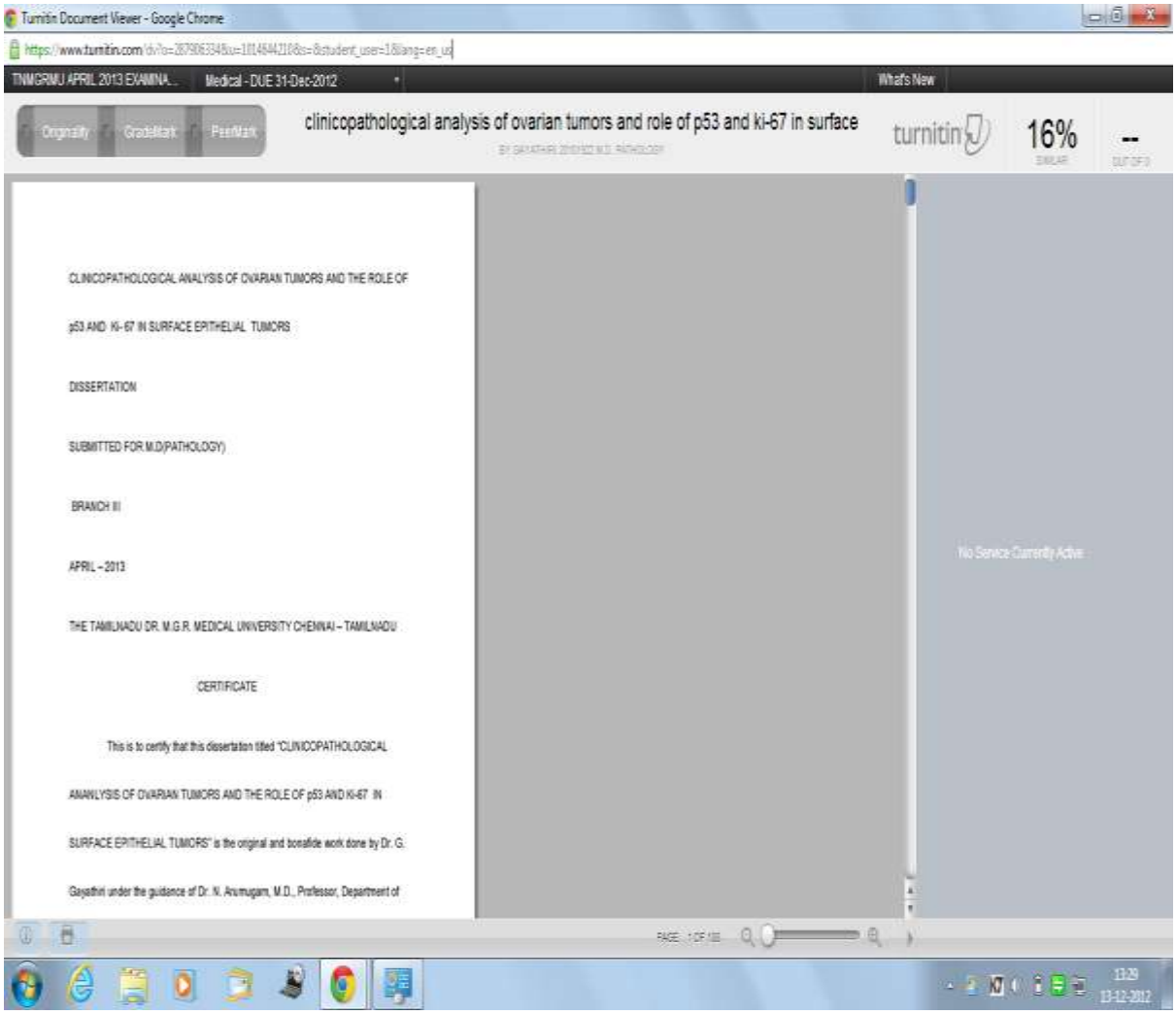
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# INTRODUCTION

# INTRODUCTION

Ovarian tumors accounts for 6% of all cancer in women[49] .Ovarian tumors are the 5th leading cause of cancer death in women in India[49]. Annual incidence rate in India is 9.0 per 100,000 population.Ovarian tumors accounts for 30% among all tumors of female genital tract [58].

Tumors of ovary generally are more prevalent in the upper socio-economic groups due to their low fertility rate and there is aracial predisposition of ovarian cancers with increased risk of Caucasians and lower risk for black women [70].

About two-thirds of ovarian tumors occurs in reproductiveage group. Many risk factors are associated with increasedprevalence of ovarian tumors most importantly ,age ,positive family history,genetic factors,hormonal and reproductive factors[42].

Most cases are sporadic, only around 5-10% of ovariancancers are Hereditary. Women having inherited mutations in BRCA-1 & BRCA2 tumor suppressor gene are at increased risk for developing the tumor [14,42].

Abdominal USG & Serum CA-125 measurement were usedas screening methods for diagnosis of early ovarian carcinoma. Fine needle aspiration cytology is used for primary diagnosis in a patient with advanced disease and also to monitor recurrences after treatment with an overall accuracy of differentiating benign from malignant ovarian tumor ranging from 90-95% [51].

Preventive measures that could be recommended onpopulation wide basis are diet modifications, cessation of smokingand prophylactic oophorectomy isusually done in patients having higher risk .[14].

Despite the development of new diagnostic andtherapeutic strategies to improve the 5- yr survival rate ,ovariancancer still remains the deadliest due to the fact that most of them are diagnosed only in advanced stages of disease where 5-yr survival rate falls less than 20% and partly it is due to paucity of knowledge about exact etiological factors[48].

Any persistent ovarian enlargement is an immediateindication for surgical assessment and actual diagnosis rests with the histopathological examination of specimen. WHO Histological Classification is used for the diagnosis of ovarian tumors. They are categorised into 3 major categories 1.Surface epithelial -stromal.2. Sex cord –stromal 3. Germ cell tumors [44,49].

Histological subtyping of surface epithelial stromal tumorsinto Benign, Borderline & Malignant has therapeutic and prognostic significance. Histological grade is an important independentprognostic factor in patients with surface epithelial stromal tumor [49].

Ovarian serous carcinoma is classified according to 2-tier grading system into low and high grade and it is based on the biological evidence that these tumors develop from different pathways of gene alterations[3]. p53 immunohistochemical staining is done to provide an update on pathogenesis of low & high grade serous carcinoma and also helps in understanding the pathogenesis of Type I & Type II ovarian carcinomas[3].

Ki-67 is a cell proliferation marker. MIB1 is a murinemonoclonal antibody against ki-67 antigen[8]. Ki-67 labelling index helps in the differential diagnosis of surface epithelial stromal tumors of ovary[34,35].

This study is undertaken in order to evaluate theincidence of ovarian neoplasms in our institution with refrerrence to age, clinicopathological features, histopathological and immunohistochemical features along with immense review of journals and research publications.

# AIM OF STUDY

# AIM OF THE STUDY

1. To study and compare the incidence of ovarian tumors in our institution along with clinical correlation.

2. To study and compare the incidence of malignant ovarian tumors in our institution in relation to malignancies occurring in female genital tract .

3. To justify the use of Two-tier grading system in ovarian serous carcinomas in routine practice.

4. To determine whether p53 mutations seperates Type I and Type II epithelial ovarian carcinomas and to provide support for new theory of ovarian carcinogenesis.

5. To determine whether Ki-67 (LI) helps in differentiating borderline and malignant surface epithelial tumors.

# MATERIALS AND METHODS

# MATERIALS AND METHODS

A total of 150 cases of ovarian neoplasms referred from Raja Mirasudhar Govt.Hospital (RMH) , Thanjavur Medical college during 2010 to 2012 were included in this study. We received unilateral, bilateral salphingo-oophorectomy along with total abdominal hysterectomy and ovariotomy specimens. Specimens were fixed in toto in 10% neutral buffered formalin and processed routinely.

In cystic ovarian neoplasms, 4-5 bits were taken from the wall alongwith papillary excrescencess if present. In solid tumors,3-4 bits were taken if the tumors were less than 5 cm. If more than 5 cm, one block per 1 cm of the tumor were taken across its greatest dimension, particularly if the appearance is variegated. 3-4 micrometre sections were cut and stained with haematoxylin and eosin (Appendix I) .

H&E stained sections were reviewed in all cases. The following clinicaland histological parametres were evaluated in particular patients age ,tumorsize,stage of disease(FIGO staging),Histological Type & Subtypes were done according to WHO Classification criteria. For serous carcinomas ,histological grade was done according to recent two-tier grading system.

The immunhistochemical detection of biomarkers in suface epithelial stromal tumors were conducted using monoclonal primary antibody (anti-ki67 and anti-P53) against Ki-67 nuclear antigen and P53 gene respectively. {Appendix II}

Ki-67 Immunostaining:

The conventional 3-4 micro metre sections were cut from paraffinblocks and the immunohistochemical staining procedure was performed using the heat induced antigen retrieval method with specific murine monoclonalantibody-MIB1 and labelling index was done. Labelling index was measured as percentage of MIB-1 positive cells in a 1000 randomly selected tumor cells.Only nuclear staining was regarded as positive; weak nuclear or cytoplasmic staining was regarded as negative.

P53 Immunostaining:

3-4 micrometre tissue sections were deparaffinised and steamed incitrate buffer for 5 minutes to facilitate antigen retrieval. The slides were then incubated with monoclonal antibody that reacts with p53 protein. Results wereinterpreted as Positive when cells shows diffuse and intense nuclear staining,Weakly stained sections are considered as negative.

# REVIEW OF LITERATURE

# REVIEW OF LITERATURE

## GROSS ANATOMY

Ovaries are paired, almond shaped pelvic organs weighing 5-8 gms. Each ovary measures 3x2x1 cm in an adult, lies on either side of uterus close to the lateral pelvic wall.[37,74]

Each ovary is attached to posterior aspect of broad ligament by the mesoovarium and is attached at its medial pole to ipsilateral uterine cornu by ovarian ligament. The lateral pole of ovary attaches to pelvic wall by infundibulopelvic ligament which contains the principal vascular supply andlymphatic drainage of the ovary[74].

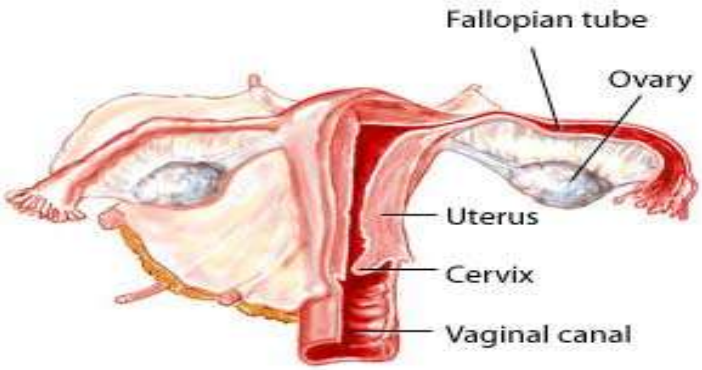
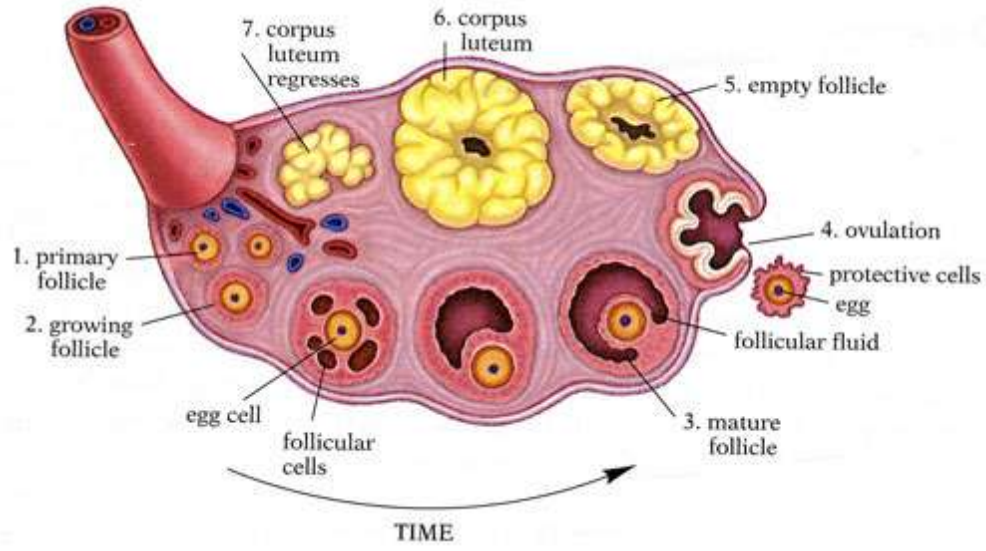



FIGURE 1: Schematic diagram of Female genital tract.

**Cut surface**

Shows narrow white outer cortex and a greyish pink,medulla thatforms the bulk of the organ. In adults,ovary shows thin walled fluid filled cystic follicles and bright yellow corpora lutea is readily visible .




**EMBRYOLOGY:**

At approximately 5 weeks of gestation; thickenings of the lining of posterior embryonic body cavity forms the genital ridges continued into the underlying primitive connective tissue known as mesenchyme, leads to the formation of primordial indifferent gonads. At 2 months of gestation, primitive gonad is recognised as an ovary because of lack of development of welldefined testicular sex cords. Mesonephric cells and germ cells remain closely associated forming ill defined ovarian sex cords embedded inprimitivemesenchyme. The coelomic epithelium remains at the periphery, enwrapping the developing ovary(37).

## HISTOLOGY:

The ovary is covered by a single layer of cells originates from the coelomic epithelium. This is a highly specialised mesothelial layer called as surface epithelium becomes continues with the mesothelium of peritonealcavity. The cells can be flattened, cuboidal, columnar or focally pseudo-stratified.

Beneath the surface epithelium lies the cortex,which is roughly divisible into outer fibrous acellular collagenous zone termed as ‘Tunica albuginea’ and inner more cellular active cortex. Inner cellular cortex contains the primordial follicle, ripening follicle and mature follicles. The stroma.consists of uniformed spindle cells in bundles often with storiform pattern(75)

The central portion of the ovary is the medulla and it also has activefollicles and cellular stroma. The blood vessels enter at the hilum areaccompanied by a small amount of connective tissue.

The hilus cell nests are unencapsulated variably sized aggregates liesin the ovarian hilar region and adjacent mesoovarium. These hilus cells are round-oval,contains abundant eosinophilic cytoplasm and vesicular nucleus & one or two nucleoli. Hilus cells contain specific crystals of Reinke, which are homogenous; eosinophilic, non refractile rod shaped structures.

## OVARIAN TUMORS:

Tumors of the ovary represents about 30% of all cancers of femalegenital tract system. Age adjusted incidence rates are highest in economically advanced countries(5).

Environmental,genetic and life style factors all influence ovarian cancer risk.Genetic susceptibility is evident from numerous epidemiological investigations and there was increased susceptibility in patients with positive family history. A number of specific genes most important of which is BRCA1and BRCA 2 . Ovarian cancer is a minor feature of the hereditary nonpolyposis colon cancer syndrome(53)

Parity, OCPs intake are associated with decreased risk for ovarian carcinomas(14). Higher risk is found to be associated with primary infertility, early menarche, late menopause ,obesity ,higher fat intake. Positive family history is strongly associated with development of ovarian cancer. Womenwhose first degree relatives have ovarian cancer have 3 times increased risk for developing the disease when compared to unaffected relatives(41).

# WHO HISTOLOGIC CLASSIFICATION OF TUMORS OF THE OVARY

## Surface epithelial – stromal

### Serous tumors

- Malignant
- Adenocarcinoma
- Borderline tumor
- Benign - Cystadenoma, adenofibroma, cystadenofibroma

### Mucinous tumors

- Malignant
- Adenocarcinoma
- Borderline tumor
- Benign - Cystadenoma,adenofibroma,cystadenofibroma
- Mucinous cystic tumor with pseudomyxoma peritonei

### Endometrioid tumors

- Malignant
- Adenocarcinoma
- Malignant mixed mullerian tumor
- Endometrial stromal sarcoma
- Borderline tumor
- Benign - Cystadenoma,adenofibroma,cystadenofibroma

### Clear cell tumors

- Malignant
- Adenocarcinoma
- Borderline tumors

- Benign - Cystadenoma , adenofibroma, cystadenofibroma

**Transitional tumors**

- Malignant
- Transitional cell carcinoma(non –Brenner type)
- Malignant Brenner tumor
- Borderline
- Benign - Brenner tumor

**Squamous cell carcinoma**

**Mixed epithelial tumors**

- Malignant
- Borderline
- Benign

**Undifferentiated and unclassified tumors**

- Undifferentiated carcinoma

- Adenocarcinoma, not otherwise specified
- **Sex cord – stromal tumors**
    - Granulosa – stromal cell tumor

✓ Granulosa cell tumor

- Adult granulosa cell tumor
- Juvenile granulosa cell tumor

Thecoma-fibroma group

- Thecoma,not otherwise specified
- Typical
- Luteinized

✓ Fibroma

- ✓ Cellular fibroma
- ✓ Fibrosarcoma
- ✓ Stromal tumor with minor sex cord elements
- ✓ Sclerosing stromal tumor
- ✓ Signet ring –stromal tumor

**Sertoli – stromal cell tumors**

Sertoli- Leydig cell tumor group

- ✓ Well differentiated
- ✓ Of intermediate differentiation
  - Variant with heterologous elements
- ✓ Poorly differentiated
  - Variant with heterologous elements
- ✓ Retiform
  - Variant with heterologous elements
- ✓ Sertoli cell tumor
- ✓ Stromal –Leydig cell tumor

✓ Sex cord –stromal tumors of mixed or unclassified cell type

- ✓ Sex cord tumor with annular tubules
- ✓ Gynandroblastoma
- ✓ Sex cord-stromal tumors,unclassified

Steroid cell tumors

- ✓ Stromal luteoma
- ✓ Leydig cell tumor group
  - Hilus cell tumor
  - Leydig cell tumor .non hilar type
  - Leydig cell tumor, not otherwise specified
- ✓ Steroid cell tumor, not otherwise specified

Well differentiated

Malignant

**Germ cell tumors**

- Primitive germ cell tumors
- Dysgerminoma
- Yolk sac tumor
- Embryonal carcinoma
- Polyembryoma
- Non gestational chorio carcinoma
- Mixed germ cell tumor
- Biphasic or triphasic teratoma
- Immature teratoma
- Mature teratoma

  -Solid

  -Cystic

  -Fetiform teratoma
- Monodermal teratoma and somatic type tumors associated with dermoid Cyst
- Thyroid tumor group

  Struma ovarii

- Benign
- Malignant
- Carcinoid tumor
- Neuro ectodermal tumor group
- Carcinoma group
- Melanocytic group
- Malignant melanoma

- ❖ Melanocytic nevus
- ❖ Sarcoma group
- ❖ Sebaceous tumor group
- ❖ Pituitary type tumor group
- ❖ Retinal anlage tumor group

**Germ cell sex cord – stromal tumor**

- ➢ Gonadoblastoma - Variant with malignant germ cell tumor
- ➢ Mixed germ cell – sex cord – stromal tumor - Variant with malignant germ cell tumor

**Tumors of the rete ovarii**

- ❖ Adenocarcinoma
- ❖ Adenoma
- ❖ Cystadenoma
- ❖ Cystadeno fibroma

**Miscellaneous tumors**

- ❖ Small cell carcinoma, hypercalcemic type
- ❖ Small cell carcinoma, pulmonary type
- ❖ Large cell neuro endocrine carcinoma
- ❖ Hepatoid carcinoma
- ❖ Primary ovarian mesothelioma
- ❖ Wilm's tumor
- ❖ Gestational choriocarcinoma
- ❖ Hydatidiform mole
- ❖ Adenoid cystic carcinoma
- ❖ Basal cell tumor
- ❖ Ovarian wolffian tumor

- ❖ Paraganglioma
- ❖ Myxoma
- ❖ Soft tissue tumors not specific to the ovary

**Tumor-like conditions**

- ❁ Luteoma of pregnancy
- ❁ Stromal hyperthecosis
- ❁ Stromal hyperplasia
- ❁ Fibromatosis
- ❁ Massive ovarian edema

**Lymphoid and haematopeitic tumors**

**Secondary tumors**

**SURFACE EPITHELIAL STROMAL TUMOR:**

Each of the tumor type is subdivided into Benign, Borderline, Malignant category. Benign tumors of serous, mucinous, endometroid, clear cell are further subtyped into cystadenoma, cystadenofibroma, adenofibromas(94).

**SEROUS TUMORS:**

The most common type of surface epithelial neoplasms areserous tumors . Approximately 60% Benign, 10% Borderline, 30% malignant(43).

**BENIGN SEROUS TUMORS:**

Occurs most commonly in $5^{th}$ decade.

**GROSS:**

They are bilateral in 10-20% cases.They are usually unilocular , entirely cystic or can be partly cystic. Cysts filled with watery thin serous fluid ,innersurface of the cyst wall can be smooth or papillary excrescences can beseen(43).

**HISTOLOGY:**

Cysts and polypoid excrescencess has single layer of ciliatedepithelium similar to that of fallopian tube. Nuclear atypia is seen. Psammoma bodies are infrequent with rare mitotic figures. Papillae when found are almost entirely made up of fibrous stroma(44).

**SEROUS BORDERLINE TUMOR:**

They are common in $4^{th}$& $5^{th}$ decade.

**GROSS**

They are bilateral in 25% of cases. They are usually cystic, containing watery or thick mucinous fluid and have surface or intracystic numerous papillary projections(28).

**HISTOLOGY:**

Three most important diagnostic features (29)are:

1. Arborising papillae (hierarchial branching) form increasingly smallerbranches ending in clusters of epithelial cells, detached from stroma .
2. Varying degree of mild –moderate nuclear atypia.
3. Absence of frank stromal invasion/solid sheets of tumor with cribriform pattern (43).

Serous borderline tumors are classified into:

1. Typical(90%)
2. Micropapillary(10%) .

Typical serous borderline tumorsmakes up the majority and has aclassic branching papillary architecture and epithelilal tufts overlying the papillae.

Micropapillary pattern shows focal or diffuse proliferation of tumor cells in elongated,thin micropapillae with little or no stromal support emergingdirectly from the cyst lining. The micropapillae are atleast five times as long asthey are wide,arising directly from the papillae with thick fibrous stalk.

Having diagnosed a serous borderline tumor following features(81) should be examined for:

1. **Surface involvement**:

   Cross examination of ovarian surface is done carefully and it is oriented such that surface is evident on slide. The presence of surface involvement are associated with increased frequency of high stage tumor. Surface involvement enables peritoneal spread.

2. **Stromal microinvasion:**

Generous and judicious sampling is required to exclude microinvasion. Atleast one section per centimetre of tumor diameteris required. Invasive foci measuring less than 10mm2 and less than 3mm2 in greatest dimension is called as microinvasion.

Microinvasive areas consist of either dyscohesive eosinophilic cells in cores of papillae. Individual cells have abundant eosinophilic cytoplasm and vesicular nuclei. Microinvasion by itself does not alter the overall behaviour of

borderline ovarian tumors,but will co-seggregate with more aggressive tumors; in which case micropapillary pattern is more ominous.

3. **Lymph node metastases:**

Pelvic and paraaortic lymphnode metastases are found in as many as 27% of cases .These metastases are present in sinusoidal spaces rather than substance of node. Its presence does not alter the prognosis of serous borderline tumors, however they have lower disease free survival.

4. **Implants on peritoneal surface:**

Implants can be invasive and non invasive. Presence of peritoneal implants and whether or not they are invasive are the most important indicators of outcome in serous borderline tumors. on invasive implants are of 2 types. Epithelial & Desmoplastic (12) .

**Epithelial implants**: implants composed of papillae resembling those within ovarian serous borderline tumor. they are found either in mesothelial lined invaginations of peritoneal surface or between the lobules of fat.

**Desmoplastic implants** : Papillae, glands, cell cluster or single cell within inflamed ;dense fibroblastic or granulation tissue that appearsto be plastered onto serosal surface.

**Invasive implant:**

1. Implants with haphazardly arranged glands involving the normal tissues such as omentum.
2. Loose or dense fibrous reaction without significant inflammation
3. Dominant epithelial proliferation
4. Nuclear features resembling low grade serous carcinoma

5. Irregular borders and
6. Aneuploidy

**SEROUS BORDERLINE ADENOFIBROMA AND CYSTADENOFIBROMA:**

In this variant epithelial lining of glands and or cysts of the adenofibroma or cystadenofibroma has the features of serous borderlinetumor instead of benign epithelium.(81)

**MALIGNANT SEROUS CYSTADENOCARCINOMA:**

**GROSS:**

They are bilateral in approximately 70% of cases. They range from microscopic size to more than 20cm dm. Mostly they are cystic and solid with papillae within cysts or on surface. Poorly differentiatedtumors are predominantly solid, multinodular masses with necrosis and haemorrhage(43)

**MICROSCOPY:**

Most serous carcinomas are high grade tumors and frequently shows obvious stromal invasion. Architecturally, tumor varies from glandular,papillary to solid pattern.glands are typically slit-like. Papillae shows irregular branching and highly cellular.poorly differentiated tumors showspredominantly solid areas. Psammoma bodies varies in number.stroma may be scanty or desmoplastic(92,103).

**GRADING:**Various grading systems are in use .The most commonly used grading system was Silverbergs grading system which is as follows (94)

**TABLE 1: Silverberg grading system:**

| Score | Architecture | Cytologic atypia | Mitotic figures/10hpf |
|---|---|---|---|
| 1 | Glandular | Mild | 0-9 |
| 2 | Papillary | Moderate | 10-24 |
| 3 | Solid | Severe | >25 |

Score 3-5: Grade 1

Score 6-7: Grade 2

Score 8-9: Grade 3

**2 –TIER GRADING SYSTEM FOR SEROUS CARCINOMA[3]:**

According to Anais Malpaica et al ,Serous carcinoma is graded according to degree of nuclear atypia and mitotic rate is used as secondary feature.

**Low grade:**

1. Mild to moderate nuclear atypia and as secondary feature

2.< 12 mitoses/10hpf.

**High grade**

1. Marked nuclear atypia and as secondary feature
2. > 12 mitoses/10 hpf and multinucleated cells.

**Significance of 2 tier grading system:**

Serous carcinomas are graded into low and high grade which reflect a difference in the pathogenesis of these tumors(3). Since the system is based on defined criteria that are easy to follow and because it involves only two diagnostic categories ,it provides better reproducibility in the grading of serous carcinoma(80).

Accordingly low grade serous carcinomas will not show p53expression as these tumors have intact p53 gene [80].In contrast more than 95%of high grade serous carcinomas shows strong positivity with p53 immunostaining indicating that this gene is involved in their tumorigenesis.

**MUCINOUS TUMORS OF OVARY**

The second most common type are mucinous tumors .About 80% ofmucinous tumors are benign,10% are borderline,10% malignant(6).

**BENIGN MUCINOUS TUMORS:**

**GROSS:**

They are large,unilateral,multilocular cystic masses containing viscous mucoid material. Cystadenofibromas are partially to almost completely solid.

**MICROSCOPY:**

Mucinous columnar epitheliumcontaining intracytoplasmic mucin lines the glands and cysts, which resembles endocervical or gastrointestinal type epithelium.Cystadenofibromas shows mucinous glands and cysts uniformly distributed in a fibromatous stroma(93).

**BORDERLINE MUCINOUS TUMORS:**

**INTESTINAL TYPE:**

**GROSS:**

About 85% of mucinous borderline ovarian tumors are of intestinal type. Bilateral in only 5% cases. They are large,cystic,multi/unilocular with viscous fluid. Borderline foci can be solid but typically reside within fleshy polypoid areas in cyst wall.(6,21)

**MICROSCOPY:**

In addition to conventional benign mucinous cystadenoma,borderlineareas shows stratification ,no more than 3 layers and may form filliformintracystic papillae with minimal support. Nuclei are enlarged hyperchromaticand have increased mitotic activity. Goblet cells are seen distributed haphazardly. Glands and cysts lumen contain mucin(6).

**ENDOCERVICAL TYPE:**

**GROSS:**

About 10-15% of borderline tumors are endocervical type. They arebilateral in 40% cases and sometimes arise within endometriotic cysts(94).

**MICROSCOPY:**

Broad bulbous papillae associated with cell stratification andepithelial tufting. The papillae are lined by both mucinous columnar cellsresembling endocervix and stratified polygonal eosinophilic cells characteristically many acute inflammatory cells are seen within thepapillae/free floating in the extracellular spaces(42).Both intestinal and endocervical type can be associated with noninvasive and invasive type implants in the peritoneum(53).

## MUCINOUS CYSTADENOCARCINOMAS

### GROSS:

Only about 5 % of these tumors are bilateral. They are large,unilateral, smooth surfaced; multilocular cystic masses containing viscous fluid. Haemorrhagic, necrotic, solid, papillary areas are relatively frequent. For all grossly suspicious areas, one histological section per 1-2 cm of tumor diameter is recommended.

### MICROSCOPY:

There are 2 forms of stromal invasion. Expansile and infiltrative. Inexpansile invasion, glands and cysts are lined by malignant cells forms complexpapillary areas or back- back arrangement of glands with little/no discernableintervening stroma. To qualify as frankly invasive, such areas should be atleast10mm2.(77)

In infiltrative type of invasion; glands, tubules, cords, cell nestshaphazardly infiltrate the stroma.The invasive cells has nondescript eosinophilic cytoplasm(77).

## MUCINOUS CYSTIC TUMOR WITH PSEUDOMYXOMA PERITONEI:

Pseudomyxoma peritonei is a clinical terminology that describe the presence of abundant gelatinous material within pelvis and abdominal cavity surrounded by fibrous tissue. First step is to exclude the presence of appendiceal neoplasm or other gastrointestinal primary mucinous tumor metastasis to peritoneum.

## ENDOMETROID TUMORS:

### BENIGN ENDOMETROID TUMORS:

**GROSS:**

These tumors average 8-10cm in dm. They are solid, firm,tan tumors with cysts of varying sizes(84).

**MICROSCOPY:**

They are well differentiated,benign appearing glands or cysts lined byendometrial type cells with or without squamous differentiation(84).

**BORDERLINE ENDOMETROID TUMORS:**

**GROSS:**

These tumors are predominantly unilateral ,ranging in size from 2-40cm; cut surface gry-white to tan,can be solid and cystic or predominantly solid. Larger tumors shows haemorrhage and necrosis(92)

**MICROSCOPY:**

Islands of crowded endometroid glands or cysts lined by cellsdisplaying grade 1 to grade 3 cytologic atypia proliferate in an adenofibromatous stroma. Absence of stromal invasion and low mitotic activity is seen. About 15-50 % of patients have endometriosis in same ovary as well as at extraovarian sites(92).

**ENDOMETROID ADENOCARCINOMAS:**

**GROSS:**

These tumors measures on an average 10-20 cm in dm, solid, friable orCysts with mass protruding into lumen. They are bilateral in about 28% cases(74)

**MICROSCOPY:**

Well differentiated tumors shows round,oval or tubular glands lined bystratified nonmucin containing epithelium. Squamous differentiation occurs in30-50% cases often in the form of morules(74).

**Table2:FIGOGrading scheme for Endometrioid adenocarcinoma:**

| Grading | Histological feature |
|---|---|
| Grade 1 or well differentiated | Well formed glands resembling villoglandular carcinoma of uterine corpus, < 5% solid tumor growth. |
| Grade 2 or moderately differentiated | More complex glandular architecture,increased nuclear stratification,6-50% solid tumor growth. |
| Grade 3 or poorly differentiated | Poorly formed glands,large sheets of cells ,> 50% solid tumor growth. |

**MALIGNANT MIXED MULLERIAN TUMOR:**

**GROSS:**

They are bilateral in 90% cases. They are large tumors partly solid andpartly cystic, bosselated masses with hemorrhage and necrosis(44).

**MICROSCOPY:**

Biphasic neoplasm that has malignant epithelial and mesenchymal component. Epithelial component can be any type of surface epithelial carcinoma.mesenchymal component most commonly seen are fibrosarcomaor endometroid stromal sarcoma or leiomyosarcoma(44).

**ADENOSARCOMA:**

**GROSS:**

Almost always unilateral and is predominantly solid with small cysts.

**MICROSCOPY:**

Biphasic tumor in which mesenchymal component is sarcomatous butepithelium is benign. Cellular stroma forms periglandular cuffing. Adenosarcoma of ovary has worse prognosis when compared to its uterinecounterpart.(44)

**ENDOMETRIAL STROMAL SARCOMA:**

**GROSS:**More than 70% tumors are unilateral. most of them are solid and firm but some have cysts filled with mucoid or haemorrhagic fluid.

**MICROSCOPY:**

More than 50% cases are associated with endometriosis. Neoplastic cells are round to oval with round nuclei and scanty cytoplasm,arrangedhaphazardly in diffuse pattern. Hallmark is the presence of abundant small thick walled vessels. These vessels are surrounded by whorls of neoplastic cells(44).

**CLEAR CELL TUMORS:**

**BENIGN TUMORS:**

**GROSS:**

External surface is smooth lobulated . Cut surfaceshows honey- combing appearance with tiny cysts embedded in rubbery stroma.(45)

**MICROSCOPY:**

Tubular glands lined by 1 or 2 layers of epithelium that containsPolygonal cells whose cytoplasm is clear with minimalnuclear atypia.(45)

**BORDERLINE CLEAR CELL TUMORS:**

**GROSS:**Smooth lobulated external surface with cut section appearing moresoftier and fleshier.

**MICROSCOPY:**Tumor composed of tubules and small cysts lined by one or several layers of cuboidal epithelial cells with clear cytoplasm or hobnail nuclei. Epithelial cells shows mild to moderate nuclear atypia and occasional mitotis(44)

**CLEAR CELL ADENOCARCINOMA:**

**GROSS:**

These tumors have an average size of about 15cm. Cut section shows unilocular cyst with yellow nodules with some cysts containing watery/mucinous fluid. They are seen associated withendometriosis ovary(44).

**MICROSCOPY:**

These tumors shows tubulocystic, papillary and solid patterns.Individual cells are polyhedral cells with abundant clear cytoplasm separated by delicate fibrovascular stroma in solid pattern(44).

**TRANSITIONAL TUMORS:**

**BENIGN BRENNER TUMOR:**

**GROSS:**

More than 50% tumors are less than 2 cm dm. They are well circumscribed firm,white gritty on sectioning with focal areas of calcification. Brenner tumors are associated with mucinous cystadenoma in about 25% Cases(76)

**MICROSCOPY:**

Nests of transitional type of epithelial cells withcentrally grooved coffee bean nuclei with abundant eosinophilic cytoplasm and distinct cell membranes. These nests lie in a predominantly fibromatous stroma.(76)

**BOREDRLINE BRENNER TUMOR:**

**GROSS:**

They are typically large with mean diameter of 16-20cm, usually has solid and cystic component.

**MICROSCOPY:**

These tumors shows branching papillae lined by transitional epithelium which protrudes into cystic spaces. There is absence ofstromal invasion. A benign Brenner component is typically present.(76)

**MALIGNANT BRENNER TUMOR:**

**GROSS:**

They are large tumors, has solid component as well as cystscontaining papillary or polypoid masses.

**MICROSCOPY:**

These tumors exhibits stromal invasion associated with a benignor borderline Brenner component. Invasive element is usually high gradetransitional cell carcinoma(93).

**TRANSITIONAL CELL CARCINOMA:**

**GROSS:**

They are bilateral in about 15% cases , often partly solid & cystic.

**MICROSCOPY:**

They have papillary architecture lined by multilayered transitional epithelium, cells shows features of malignancy and these tumorsshould not have a benign or borderline Brenner component.(93)

**MIXED EPITHELIAL TUMOR:**

**MICROSCOPY:**

These tumors consists of admixture of 2 or more of 5major cell types: serous, endometroid, clear cell, Mucinous and transitional.(76)

**UNDIFFERENTIATED CARCINOMA:**

**MICROSCOPY:**

It is a primary ovarian tumor with no differentiation and marked cytological atypia.(76)

**B. SEX CORD – STROMAL TUMOR :**

**GRANULOSA CELL TUMOR:**

These tumors constitute for about 1.5% of all tumors of ovary(76).

**ADULT TYPE:**

**GROSS:**

They are unilateral in 95% of cases. On an average size of 12 cm and encapsulated. Cut section shows solid and cystic,areas of necrosis and haemorrhage giving a variegated appearance.(1)

**MICROSCOPY:**

There is proliferation of granulosa cells often with a stromal component of fibroblasts, theca or lutenised cells. Individual cells have scanty cytoplasm with longitudinal nuclear grooves. There is minimal to no cytological atypia and a low mitotic activity (1,76).

These tumors shows different histological patterns including microfollicular, macrofollicular, watered silk, gyriform and diffuse. (1,76).Mostcommon pattern is microfollicular characterised by the presence of call-exnerbodies. Fibrothecomatous stroma often surrounds granulosa cells.

**JUVENILE TYPE:**

Occurs predominantly before 30 yrs age group . In prepubertalgirls 90% are associated with isosexual pseudo precocity.(76)

**GROSS:**

These tumors are indistinguishable from adult type granulosa cell tumor .

**MICROSCOPY:**

These tumors shows nodular or diffuse cellular growth punctuatedby macrofollicles of varying sizes and shapes. Their lumen contain eosinophilic or basophilic fluid. Typically rounded neoplastic granulosa cells has abundant eosinophilic and or vacuolated cytoplasm and almost all nuclei lack grooves. Abundant mitotic figures seen.(1,76)

**THECOMA –FIBROMA:**

**THECOMA**

**GROSS:**

These tumors occur in postmenopausal women .They have anaverage size of about 5-10 cm. Cut section shows solid and yellow and almost always unilateral.(93)

**MICROSCOPY:**

Tumor cells are uniform ,bland oval to spindle shaped nuclei with abundant pale vacuolated lipid rich cytoplasm. Individual cells are invested by reticulin. Mitoses are absent. Calcifications are commonly seen .Luteinised

thecomas contain lutein cells ,individually or in nests, in a background more often fibromatous than thecomatous. Oedema and microcyst formation is striking(93).

**FIBROMA:GROSS:**

They account for 4% of all ovarian tumors.they are hard whitetumors. Majority of them are unilateral.(40). About 10-15% of tumors are large and often associated with ascites and Meigs syndrome(4).

**MICROSCOPIC:**

These tumors composed of spindle shaped cells with uniform bland nuclei and scant cytoplasm, arranged in fascicles or in a storiform pattern. Mitoses are absent. About 10% are uniformly and densely cellular and are referred as cellular fibromas.(4,40)

**FIBROSARCOMA:**

**GROSS:**

Large, solid tumors, haemorrhagic and necrotic and usually unilateral.

**MICROSCOPIC:**

These tumors are densely cellular with moderate to severecytological atypia, high mitotic rate and atypical mitotic figures with haemorrhage and necrosis.(94)

**SCLEROSING STROMAL TUMOR:**

**GROSS:**They are typically unilateral and well circumscribed averaging 15cm in dm. Cut section shows solid,grey white with occasional yellow foci(94).

**MICROSCOPY:**

These tumors shows pseudolobulation of cellular areasseparated by hypocellular areas of densely collagenous stroma. Cellular areas shows prominent thin walled vessels, some of them having HPC-like pattern.

**SIGNET-RING STROMAL TUMOR :**

**GROSS:**

These tumors may be both solid and cystic or uniformly solid.

**MICROSCOPY:**

H& E section shows a diffuse proliferation of spindle and round cells, latter shows eccentric nuclei with a single large intracytoplasmic vacuole and resemble signet ring cells(93).

**SERTOLI-STROMAL CELL TUMOR:**

**SERTOLI-LEYDIG CELL TUMOR GROUP:**

They are rare and comprises of less than 0.5% of all ovarian tumors.

**GROSS:**Majority of them are unilateral.they are solid or solid and cystic.Solid areas are fleshy,pale yellow with areas of haemorrhage and necrosis.(94)

**MICROSCOPY:**

1. Well differentiated(Meyer's type I) tumors, sertoli cells are present in open or closed tubules and lack significant nuclear atypia or mitotic activity.

2. Intermediate,( Meyer's type II)- Composed of cords, sheets and nests of sertoli like cells separated by spindle stromal cells
3. Poorly differentiated( sarcomatoid ,Meyers type III)-they are arranged in sarcomatoid pattern with masses of spindle shapedcells.(94)

**SERTOLI CELL TUMOR:**

They are commonly seen in women of reproductive age group.

**GROSS:**

Pure forms of sertoli cell tumors are rare. They are mostly unilateraland average size of 5-7 cm diametre in size.(76)

**MICROSCOPY:**

These tumors composed of sertoli cells that line tubules or trabeculaeor grow in nests or solid sheets. Cells are columnar or polygonal and have small round to oval nuclei and granular or eosinophilic cytoplasm, with minimal nuclear atypia. (76).

**GYNANDROBLASTOMA:**

Gynandroblastoma is a rare tumor ,containing both sertoli cells orsertoli-leydig cell and granulosa cell differentiation. They are usually unilateral with size ranging from 1-18cm. Microscopically tubules and trabeculae similarto those in well differentiated sertoli or sertoli-leydig cell tumors mixed with nests and sheets of granulosa cells.(76)

**STEROID CELL TUMOR:**

**GROSS:**

They are large and usually well circumscribed often lobulated appearance. Sectioned surface ranges from yellow to brown or black.

**MICROSCOPY:**

These tumors shows solid aggregates of cells withoccasional nests or trabeculae. Tumor cells are polygonal with granular and eosinophilic cytoplasm,nuclei are usually bland. Areasof haemorrhage and necrosis can be seen(94).

## C. GERM CELL TUMORS:

**INTRODUCTION :**

These tumors account for 30% of primary neoplasms of ovary, 95% of which are dermoid cysts(mature cystic teratomas). Median age at presentation is 18 years. Malignant GCT are common cancers among children and adolescent females. (94)

**DYSGERMINOMAS:**

**GROSS:**

Well encapsulated tumor ,unilateral in 90% of cases. Average tumor size is 15cm dm. Section shows solid,uniform or lobular and creamy white. Foci of coagulative necrosis and cystic change or macroscopic calcification can be seen.(15)

**MICROSCOPY:**

Tumor shows sheets of monotonous appearing polygonal cells with abundant pale cytoplasm and fairly uniform vesicular nuclei with prominent nucleoli. Tumor cells found in lobules separated by thin fibrous septainfiltrated

with lymphocytes. syncytiotrophoblastic cells are found in around 5% of cases.(15)

**YOLK SAC TUMOR:**

**GROSS:**

They are well encapsulated tumor with an average size of 15cm dm.Cut section shows grey yellow areas with frequent areas of necrosis, haemorrhage and liquefaction. Cysts are also seen.(39)

**MICROSCOPY:**

Tumor shows the characteristic reticular pattern formed by aloose, myxoid stroma harbouring a network of microcysts. These cysts are lined by clear or flattened epithelial cells. PAS +ve hyaline globules are seen tumor. Only around 10-20% of tumors shows schiller-duval bodies.(39)

**EMBRYONAL CARCINOMA AND POLYEMBRYOMA:**

They are rare tumors mostly reported as a component of mixedgerm cell tumors.(46)

**MICROSCOPY:**

Tumor shows dysorganised sheets of large primitive appearing cells forming papillae or crevices coexist with syncytiotrophoblastic cells as well as early teratoid differentiation.When abundant embryoid bodies are seenthis tumor is called as Polyembryoma .(46)

**MIXED GERM CELL TUMOR:**

These tumors are composed of atleast 2 different germ cellcomponents of which atleast one is primitive.(46)

**MICROSCOPY:**

Most common combination found is yolk sac tumor anddysgerminoma. Some of the additional elements are immature/mature teratoma, polyembryoma, embryonal carcinoma, may be present.(46)

**BIPHASIC TERATOMA:**

These are tumors composed of derivatives of 2 or 3 germ layers.

**IMMATURE TERATOMA:**

**GROSS:**

Typically unilateral ,large,variegated predominantly solid.

**MICROSCOPY:**

Tumor shows immature embryonal type tissues, in the form of neuroepithelial rosettes and tubules admixed with mature tissue.

**MATURE TERATOMA:**

Most mature cystic teratomas occur in the reproductive agegroup. Mature solid teratomas occur mainly in first two decades of life.(76)

**GROSS:**

Dermoid cysts presents as cystic mass with an average size of 15cm dm, they are bilateral in 8-15% of cases. Cysts are often filled with hair and sebaceous material. Rokitansky protruberance is seen protruding into the cyst(76).

**MICROSCOPY:**

Tumor shows mature tissue from all three germ layers. most commonly squamous epithelium,sweat glands ,sebaceous glands. Mesodermalelements like

smooth muscle, teeth, bone, respiratory epithelium, gastrointestinal epithelium are also seen.(76)

**MONODERMAL TERATOMAS:**

**STRUMA OVARII:**

Most common type of monodermal teratoma. Accounts for 2-7% of all ovarian teratomas.(92)

**GROSS:**

They are unilateral and size varies from 0.5-10 cm dm. Cut section brown solid and gelatinous nodules within a dermoid cyst(92).

**MICROSCOPY:**

Tumor is composed of normal or hyperplastic thyroid tissue withmicro or macrofollicular pattern trabecular and solid pattern. Most common malignancy in struma ovarii is papillary carcinoma with similar characteristichistological features as in tumors arising from thyroid gland.(92)

**CARCINOID TUMOR:**

Ovarain carcinoids account for 0.5-1.7% of all carcinoids(63).

**GROSS:**Primary ovarian carcinoids are unilateral and present as firm,tannodule protruding into dermoid cysts. Cut section shows firm homogenous and tan to yellow(63).

**MICROSCOPY:** Insular carcinoid consists of islands and nests of round cells withabundant eosinophilic cytoplasm and round uniform nuclei. Trabecularcarcinoids exhibits wavy and anastomosing ribbons composed of columnarcells with long axes ofcell parallel to one another(63).

**NEUROECTODERMAL TUMOR:**

**GROSS:**They are unilateral and an average size of 14 cm dm. Sectioned surfaceis solid with friable, gray pink ,tissue and cysts with papillary excrescencess. (85)

**MICROSCOPY:** Well differentiated tumors forms like ependymomas and poorlydifferentiated tumors like medulloepithelioma and primitive neuro ectodermaltumor are seen. Anaplastic forms such as glioblastoma multiforme is alsoseen(85).

**CARCINOMA:** Carcinoma secondarily develops from dermoid cysts. They usually occur in postmenopausal women(46).

**GROSS:**Cauliflower like exophytic growth or infiltrative grey white plaqueswith necrosis and haemorrhage may be seen.

**MICROSCOPY:**Most common type of carcinoma arises is squamous cell carcinoma accounting for 80% of cases. Second most common malignancy isadenocarcinoma.(46)

**SARCOMAS:**

**MICROSCOPY:**Accounts for 8% of cases of malignancy in dermoid cyst. Most cases are leiomyosarcoma, angiosarcoma, osteosarcoma, chondrosarcoma, fibrosarcoma.

**MELANOCYTIC TUMORS:**They are rare tumors , dermoid cyst with melanoma in stage I are alive even after 2 yrs of diagnosis .(92).

**SEBACEOUS TUMORS:**

**MICROSCOPY:**Tumors like basal cell carcinoma with sebaceous differentiation, sebaceous carcinoma and sebaceous adenoma are common. Hallmark ofthese lesions is presence of large number of mature sebaceous cells with oil red O positive staining.(76)

**PITUITARY TYPE TUMORS:**Corticotroph cell adenoma and prolactinomas are common(76).

**RETINAL ANLAGE TUMOR:** Pigmented progonoma and malignant tumors derivedfrom the retinal anlage are seen.(95)

**GERM CELL-SEX CORD STROMAL TUMOR(93): GONADOBLASTOMA:**

Most of these patients have gonadal dysgenesis and more than 90% cases have a Y chromosome.Typically seen in children or young adults.gonadoblastoma is a benign tumor unless a malignant germ cell component is seen.(93)

**GROSS:**They are small with a yellow to tan grey cut surface and areas ofcalcification.(93)

**MICROSCOPY:**Tumor is composed of 2 main cell types; germ cell similar to that ofdysgerminoma or seminoma and sexcord derivatives resembling immature sertoli cells. The stroma contains a lutenised orleydig –like cells devoid of reinke crystal. (93)

**MIXED GERM CELL-SEX CORD-STROMAL TUMOR:**

Occurs in infants or children under the age of 10. One fourth of cases have isosexual pseudoprecocity.(94)

**GROSS:**They are large tumors predominantly solid or partly solid &cystic.

**MICROSCOPY:**Tumor is composed of germ cells and sexcord derivatives similar in apperaence to immature sertoli/ granulosa cells intimately admixed with each other.(94)

**D: TUMORS OF RETE OVARII:**Most of these lesions are incidental finding in a postmenopausal women.To diagnose, these lesions tumor must be located in ovarian hilus.(16)

**MICROSCOPY:**Tumor is composed of cuboidal cells or columnar nonciliated cells arranged in retiform spaces.dilated areas and cyst are most frequently seen.(16)

**METASTATIC TUMORS:**These tumors comprise about 5-10% of all ovariantumors. Primary tumors from gastrointestinaltract (especially large intestine, stomach, appendix), are most common followed by Breast, Uterine corpus and uterine cervix. In young girls ovarian metastases are common with neuroblastoma, rhabdomyosarcoma, Ewing sarcoma. (82,98).

**GENERAL FEATURES OF OVARIAN METASTASES:**

1. Bilaterality.
2. Small superficial; Multinodular tumor
3. Vascular invasion
4. Desmoplastic reaction
5. Extensive unusal extraovarian spread
6. Unusual clinical history.

**GROSS:**Ovarian metastases are bilateral in 70% of cases. Size of ovarian metastase varies from microscopic size to more than 10cm(16).

**MICROSCOPY:**Metastatic tumors grow as superficial or parenchymatous solid nodules. Histologic nature depends on the primary tumor(16).

**KRUKENBERG TUMOR:**They are defined characterised by thepresence of mucin –filled,signet ring tumor cells within cellular stroma of the ovary. Most krukenberg tumors represent ovarian metastases from the gastrointestinal tract, especially stomach(59).

**p53:**

p53 is a tumor suppressor gene situated on chromosome 17[45]P53 gene mutation results in uncontrolled cell proliferation. Approximately 50% of malignant tumors in humans have mutations in p53 gene and it is the Most common tumor suppressor gene involved with human malignancies.(66)

Studies have shown that p53 gene is mutated in about 50 - 80% ofovarian carcinomas[31]. It has been identified that immunohistochemical detection of p53 protein overexpression, is an adverse prognostic factor for survival in human ovarian cancer[67].

The number of cases with mutant Tp53 among ovarian serous and endometroid carcinomas is 57% and 25% respectively with maximum value in the poorly differentiated tumors in patients with stage III or stage IV disease.One of the reasons for deranged p53 gene functions can be related to BRCA1 & BRCA2 mutations which are frequent event in hereditary ovarian Carcinoma[66].

Ovarian low grade serous carcinomas evolve from borderlinetumors and they lack p53 mutations but they often have mutations of KRAS & BRAF gene mutations(Type I pathway).In contrast ovarian high grade serous carcinomas

arise as denovo and majority of them has p53 mutations and lack KRAS, BRAF gene mutations(Type II pathway)[17].Epithelial ovarian malignancies showing p53 aberrations aresignificantly less sensitive to chemotheraphy and more aggressive than those with functional p53 gene.[7]

**Ki-67:**

Ki-67 is a cell proliferation marker. Ki-67 antigen immunostaining isused to estimate the proliferation index of a tumor[34]. This antigen ispreferentially expressed in late G1,S,G2& M phase except in G0 phase[8]

Determining the proliferative activity of ovarian tumors has reportedto be of diagnostic and prognostic value[22,34]. In paraffin section, MIB1 antibody is equivalent to ki-67. MIB1 is a murine monoclonal antibody reacts withthe Ki-67 protein expressed by the proliferating tumor cells[23].

MIB1 antibody staining provide a reliable means of identifyingproliferating normal and neoplastic human cells in histological sections[89,99].

Ki-67 immunostaining in ovarian malignancies is helpful in differentiatingborderline and malignant surface epithelial tumors of ovary.(22,27)

# MASTER CHART

# MASTER CHART

| Sl.No | HPE.No | AGE-YRs | CLINICAL PRESENTATION | GROSS FEATURE | HPE DIAGNOSIS | FIGOSTAGING |
|---|---|---|---|---|---|---|
| 1. | 1/10 | 47 | MASS ABDOMEN | UNILATERAL-CYSTIC | BENIGN serous CYSTADENOMA | I |
| 2. | 66/10 | 45 | MASS ABDOMEN | UNILATERAL-CYSTIC | BENIGN SEROUS CYSTADENOMA | I |
| 3. | 96/10 | 25 | PREGNANCY ASSOCIATED | UNILATERAL-CYSTIC | MATURE CYSTIC TERATOMA | I |
| 4. | 232/10 | 24 | MASS ABDOMEN | UNILATERAL-CYSTIC | BENIGN SEROUS CYSTADENOMA | I |
| 5. | 258/10 | 28 | MASS ABDOMEN | UNILATERAL – CYSTIC | MATURE CYSTIC TERATOMA | I |
| 6. | 314/10 | 50 | ASYMPTOMATIC | UNILATERAL-CYSTIC | BENIGN SEROUS CYSTADENOMA | I |
| 7. | 337/10 | 21 | MASS ABDOMEN | UNILATERAL-CYSTIC | BENIGN SEROUS CYSADENOMA | I |
| 8. | 425/10 | 42 | MASS ABDOMEN | UNILATERAL-CYSTIC | MATURE CYSTIC TERATOMA | I |
| 9. | 442/10 | 50 | MASS ABDOMEN WITH ASCITES | BILATERAL, SOLID&CYSTIC | BILATERAL PAPILLARY SEROUS CYSTADENOCARCINOMA | III |
| 10. | 528/10 | 27 | MASS ABDOMEN | UNILATERAL – CYSTIC | BENIGN serous CYSTADENOMA | I |
| 11. | 589/10 | 40 | MASS ABDOMEN | UNILATERAL-CYSTIC | BENIGN SEROUS CYSTADENOMA | I |
| 12. | 613/10 | 33 | MASS ABDOMEN | UNILATERAL-CYSTIC | MATURE CYSTIC TERATOMA | I |
| 13. | 824/10 | 46 | MASS ABDOMEN | UNILATERAL-CYSTIC | MATURE CYSTIC TERATOMA | I |
| 14. | 1001/10 | 42 | MASS ABDOMEN | R-SOLID, L-CYSTIC | R-BENIGN BRENNER,L-BENIGN MUCINOUS CYSTADENOMA | I |
| 15. | 1023/10 | 42 | ASYMPTOMATIC | UNILATERAL-CYSTIC | BENIGN serous CYSTADENOMA | I |
| 16. | 1025/10 | 23 | MASS ABDOMEN | UNILATERAL-CYSTIC&SOLID | GRANULOSA CELL TUMOR | I |
| 17. | 1031/10 | 32 | MASS&PAIN ABDOMEN | UNILATERAL-CYSTIC HAEMORHAGIC FLUID | CONGESTED SEROUS CYSTADENOMA | I |
| 18. | 1096/10 | 45 | MASS ABDOMEN | R-CYSTIC,L-CYST WITH PAPILLARY EXCRESENCES | R-BORDERLINE MUCINOUS CYSTADENOMA L-SEROUS PAPILLARY CYSTADENOMA | I |
| 19. | 1107/10 | 40 | PAIN ABDOMEN | UNILATERAL- | CONGESTED | I |

| | | | | | | |
|---|---|---|---|---|---|---|
| | | | | CYSTIC,HAEMORRHAGIC FLUID | SEROUS CYSTADENOMA | |
| 20. | 1173/10 | 39 | MASSABDOMEN ,ASCITES | BILATERAL,SOLID | KRUKENBERG TUMOR | |
| 21. | 1181/10 | 25 | MASS ABDOMEN | UNILATERAL-CYSTIC | BENIGN SEROUS CYSTADENOMA | I |
| 22. | 1314/10 | 34 | ASYMPTOMATIC | UNILATERAL-CYSTIC | BORDERLINE MUCINOUS CYSTADENOMA | I |
| 23. | 1362/10 | 12 | MASS ABDOMEN | UNILATERAL-SOLID,CYSTIC,VARIEGATED | MIXED GERM CELL TUMOR | I |
| 24. | 1364/10 | 60 | MASS ABDOMEN | BILATERAL,CYST WITH PAPILLARY EXCRESCENCE | BILATERAL BENIGN SEROUS CYSTADENOFIBROMA | I |
| 25. | 1459/10 | 40 | MASS ABDOMEN | UNILATERAL CYSTIC WITH PAPILLARY EXCRESCENCE | BENIGN SEROUS CYSTADENOMA | I |
| 26. | 1553/10 | 70 | MASS ABDOMEN | UNILATERAL CYSTIC | BENIGN SEROUS CYSTADENOMA | I |
| 27. | 1606/10 | 22 | MASS ABDOMEN | UNILATERAL CYSTIC | BENIGN SEROUS CYSTADENFIBROMA | I |
| 28. | 1643/10 | 47 | MASS ABDOMEN | UNILATERAL-CYSTIC,SOLID,VARIEGATED | GRANULOSA CELL TUMOR | I |
| 29. | 1654/10 | 58 | MASS ABDOMEN | UNILATERAL-CYSTIC | BENIGN SEROUS CYSTADENOMA | I |
| 30. | 1656/10 | 38 | MASS ABDOMEN | UNILATERAL SOLID,CYSTIC,VARIEGATED | GRANULOSA CELL TUMOR | II |
| 31. | 1698/10 | 29 | MASS ABDOMEN | UNILATERAL-CYSTIC | BENIGN serous CYSTADENOMA | I |
| 32. | 1763/10 | 50 | MASS ABDOMEN | UNILATERAL,SOLID,CYSTIC,VARIEGATED | GRANULOSA CELL TUMOR | I |
| 33. | 1809/10 | 70 | MASS ABDOMEN, ASCITES | BILATERAL,SOLID,CYSTIC,VARIEGATED | BILATERAL PAPILLARY SEROUS ADENO CARCINOMA | II |
| 34. | 1853/10 | 27 | PAIN ABDOMEN | UNILATERAL CYSTIC | MATURE CYSTIC TERATOMA | I |
| 35. | 1892/10 | 24 | MASS ABDOMEN | UNILATERAL CYSTIC | BENIGN SEROUS CYSTADENOMA | I |
| 36. | 1894/10 | 28 | MASS ABDOMEN | UNILATERAL CYSTIC | BENGN SEROUS CYSTADENOMA | I |
| 37. | 1934/10 | 50 | MASS ABDOMEN | UNILATERAL,CYSTIC | MATURE CYSTIC TERATOMA | I |

| | | | | | | |
|---|---|---|---|---|---|---|
| 38. | 1985/10 | 52 | MASS ABDOMEN | UNILATERAL - CYSTIC | MATURE CYSTIC TERATOMA | I |
| 39. | 2024/10 | 26 | MASS ABDOMEN | UNILATERAL - CYSTIC | MATURE CYSTIC TERATOMA | I |
| 40. | 2050/10 | 50 | MASS ABDOMEN | UNILATERAL CYSTIC | MATURE CYSTIC TERATOMA | I |
| 41. | 2107/10 | 23 | MASS ABDOMEN | UNILATERAL CYSTIC | MATURE CYSTIC TERATOMA | I |
| 42. | 2119/10 | 29 | MASS ABDOMEN | UNILATERAL SOLID | FIBROMA | I |
| 43. | 2124/10 | 40 | MASS ABDOMEN | UNILATERAL- CYSTIC | MATURE CYSTIC TERATOMA | I |
| 44. | 2151/10 | 45 | MASS ABDOMEN | UNILATERAL- CYSTIC | BORDERLINE MUCINOUS CYSTADENOMA | I |
| 45. | 2165/10 | 24 | PAIN&MASS ABDOMEN | UNILATERAL- CYSTIC,HAEMO RRHAGIC FLUID | BENIGN SEROUS CYSTADENOMA | I |
| 46. | 2358/10 | 65 | MASS ABDOMEN | UNILATERAL CYSTIC | BENIGN MUCINOUS CYSTADENOMA | I |
| 47. | 2438/10 | 48 | MASS ABDOMEN, ASCITES | BILATERAL, SOLID,CYSTIC, HAEMORHAGIC | BILATERAL SEROUS ADENO CARCINOMA | II |
| 48. | 2499/10 | 50 | MASS ABDOMEN | UNILATERAL, CYSTIC | BORDERLINE MUCINOUS CYSTADENOMA | I |
| 49. | 2605/10 | 35 | MASS ABDOMEN | UNILATERAL, SOLID,CYSTIC | MUCINOUS CYSTADENO CARCINOMA | I |
| 50. | 2611/10 | 54 | MASS ABDOMEN | UNILATERAL CYSTIC | BENIGN SEROUS CYSTADENOMA | I |
| 51. | 2634/10 | 36 | PAIN ABDOMEN | UNILATERAL CYSTIC | BENIGN SEROUS CYSTADENOMA | I |
| 52. | 2666/10 | 35 | MASS ABDOMEN | UNILATERAL, CYSTIC | BENIGN SEROUS CYSTADENOMA | I |
| 53. | 2722/10 | 40 | MASS ABDOMEN | UNILATERAL, CYSTIC | BENIGN SEROUSCYSTADE NOMA | I |
| 54. | 2723/10 | 32 | PAIN&MASS ABDOMEN | UNILATERAL, CYSTIC, HAEMORHAGIC FLUID | BENIGN SEROUS CYSTADENO FIBROMA. | I |
| 55. | 2799/10 | 60 | MASS ABDOMEN | UNILATERAL CYSTIC | BORDERLINE MUCINOUS CYSTADENOMA | I |
| 56. | 2906/10 | 63 | MASS ABDOMEN | UNILATERAL SOLID | FIBROMA | I |
| 57. | 2911/10 | 21 | PAIN&MASS ABDOMEN | UNILATERAL – CYSTIC HAEMORHAGIC | CONGESTED SEROUS CYSTADENOMA | I |

| | | | | | | |
|---|---|---|---|---|---|---|
| | | | | FLUID | | |
| 58. | 3067/10 | 32 | MASS ABDOMEN | UNILATERAL-CYSTIC | BENIGN SEROUSCYSTADENOMA | I |
| 59. | 3136/10 | 38 | MASS ABDOMEN | UNILATERAL SOLID& CYSTIC, VARIEGATED | SEROUS CYST ADENO CARCINOMA | III |
| 60. | 3198/10 | 60 | MASS ABDOMEN | BILATERAL, R& L-CYSTIC | R- SEROUS CYSTADENOMA L-MATURE CYSTIC TERATOMA | I |
| 61. | 3223/10 | 26 | MASS ABDOMEN | UNILATERAL-CYSTIC | MATURE CYSTIC TERATOMA | I |
| 62. | 3257/10 | 60 | MASS ABDOMEN, ASCITES | UNILATERAL, SOLID,CYSTIC, PAPILLARY EXCRESCENCES | SEROUS CYSTADENO CARCINOMA | III |
| 63. | 3288/10 | 45 | PAIN ABDOMEN | UNILATERAL, CYSTIC,SOLID, VARIEGATED | GRANULOSA CELL TUMOR | I |
| 64. | 3417/10 | 40 | PAIN ABDOMEN | UNILATERAL CYSTIC,HAEMORRHAGIC FLUID | CONGESTED SEROUS CYSTADENOMA | I |
| 65. | 3454/10 | 21 | PAIN ABDOMEN WITH ECTOPIC PREGNANCY | UNILATERAL , CYSTIC | MATURE CYSTIC TERATOMA | I |
| 66. | 3528/10 | 38 | MASS ABDOMEN | UNILATERAL-SOLID,CYSTIC, VARIEGTAED | GRANULOSA CELL TUMOR | I |
| 67. | 3529/10 | 48 | MASS ABDOMEN, ASCITES | UNILATERAL, SOLID , CYSTIC , PAPILLARY EXCRESCENCESS ,NECROSIS | PAPILLARY SEROUS CYSTADENO CARCINOMA | III |
| 68. | 3544/10 | 26 | MASS ABDOMEN | UNILATERAL, CYSTIC | SEROUS CYSTADENOMA | I |
| 69. | 3601/10 | 50 | MASS ABDOMEN | UNILATERAL, SOLID,CYSTIC, VARIEGATED | GRANULOSA CELL TUMOR | I |
| 70. | 3619/10 | 55 | MASS ABDOMEN | UNILATERAL, SOLID,CYSTIC | GRANULOSA CELL TUMOR | I |
| 71. | 3669/10 | 42 | MASS ABDOMEN | UNILATERAL, CYSTIC | BENIGN MUCINOUS CYSTADENOMA | I |
| 72. | 3708/10 | 35 | MASS ABDOMEN | UNILATERAL CYSTIC | BENIGN MUCINOUS CYSTADENOMA | I |
| 73. | 3760/10 | 35 | MASS ABDOMEN | UNILATERAL,CYSTIC | BENIGN MUCINOUS CYSTADENOMA | I |
| 74. | 3834/10 | 45 | MASS ABDOMEN | UNILATERAL,CY | BENIGN | I |

| | | | | | | |
|---|---|---|---|---|---|---|
| | | | | STIC | MUCINOUS CYSTADENOMA | |
| 75. | 3837/10 | 58 | ASYMPTOMATIC | UNILATERAL,CYSTIC WITH PAPILLARY EXCRESCENCESS | BENIGN SEROUS ADENOFIBROMA | I |
| 76. | 3860/10 | 40 | MASS ABDOMEN | UNILATERAL CYSTIC | BENIGN MUCINOUS CYSTADENOMA | I |
| 77. | 3922/10 | 40 | MASS ABDOMEN | UNILATERAL CYSTIC | PAPILLARY SEROUS CYSTADENO FIBROMA | I |
| 78. | 3927/10 | 26 | MASS ABDOMEN | UNILATERAL CYSTIC | BENIGN MUCINOUS CYSTADENOMA | I |
| 79. | 3938/10 | 50 | MASS ABDOMEN | UNILATERAL CYSTIC WITH PAPILLARY EXCRESCENCESS | PAPILLARY SEROUUS CYSTADENO FIBROMA | I |
| 80. | 3945/10 | 28 | MASS ABDOMEN | UNILATERAL CYSTIC PAPILLARY EXCRESCENCESS | PAPILLARY SEROUS CYSTADENO FIBROMA | I |
| 81. | 4005/10 | 28 | MASS ABDOMEN | UNILATERAL CYSTIC | MATURE CYSTIC TERATOMA | I |
| 82. | 4183/10 | 30 | MASS ABDOMEN | UNILATERAL, CYSTIC | PAPILLARY SEROUS CYSTADENO FIBROMA | I |
| 83. | 4247/10 | 37 | MASS ABDOMEN | UNILATERAL CYSTIC | MUCINOUS CYSTADENOMA | I |
| 84. | 4275/10 | 27 | MASS ABDOMEN | UNILATERAL SOLID AND CYSTIC | MUCINOUS CYSTADENO CARCINOMA | I |
| 85. | 4352/10 | 28 | MASS ABDOMEN | UNILATERAL, CYSTIC | MUCINOUS CYSTADENOMA | I |
| 86. | 4473/10 | 23 | MASS ABDOMEN | UNILATERAL, CYSTIC | MATURE CYSTIC TERATOMA | I |
| 87. | 133/11 | 22 | MASS ABDOMEN | UNILATERAL CYSTIC | PAPILLARY SEROUS CYSTADENO FIBROMA | I |
| 88. | 181/11 | 50 | MASS ABDOMEN | UNILATERAL,SOLID, CYSTIC | SEROUS CYSTADENOCARCINOMA | II |
| 89. | 294/11 | 45 | MASS ABDOMEN | UNILATERAL, CYSTIC | BORDERLINE MUCINOUS CYSTADENOMA | I |
| 90. | 369/11 | 19 | PAIN ABDOMEN | UNILATERAL | BENIGN | I |

| | | | | | | |
|---|---|---|---|---|---|---|
| | | | | CYSTIC,HAEMORRHAGIC FLUID | MUCINOUS CYSTADENOMA | |
| 91. | 493/11 | 21 | PAIN ABDOMEN | UNILATERAL, CYSTIC,HAEMORRHAGIC FLUID | BENIGN SEROUS CYST | I |
| 92. | 604/11 | 27 | PREGNANCY ASSOCIATED | UNILATERAL CYSTIC | MATURE CYSTIC TERATOMA | I |
| 93. | 642/11 | 45 | MASS ABDOMEN | UNILATERAL , CYSTIC | MUCINOUS CYSTADENOMA | I |
| 94. | 644/11 | 30 | MASS ABDOMEN | UNILATERAL CYSTIC | MUCINOUS CYSTADENOMA | I |
| 95. | 700/11 | 32 | MASS ABDOMEN | UNILATERAL, CYSTIC | MUCINOUS CYSTADENOMA | I |
| 96. | 758/11 | 35 | MASS ABDOMEN | UNILATERAL, CYSTIC WITH PAPILLARY EXCRESCENCESS | PAPILLARY SEROUS CYSTADENO FIBROMA | I |
| 97. | 760/11 | 50 | MASSABDOMEN ,ASCITES | UNILATERAL SOLID AND CYSTIC | MUCINOUS CYSTADENO CARCINOMA | I |
| 98. | 1023/11 | 26 | ASYMPTOMATIC | UNILATERAL CYSTIC | BENIGN SEROUS CYSTADENOMA | I |
| 99. | 1035/11 | 31 | MASS ABDOMEN | UNILATERAL, CYSTIC | BENIGN MUCINOUS CYSTADENOMA | I |
| 100. | 1217/11 | 47 | MASS ABDOMEN | UNILATERAL, CYSTIC | BENIGN MUCINOUS CYSTADENOMA | I |
| 101. | 1381/11 | 50 | MASS ABDOMEN | BILATERAL SOLID | BILATERAL KRUKENBERG TUMOR | |
| 102. | 1481/11 | 50 | MASS ABDOMEN | UNILATERAL, SOLID,CYSTIC | PAPILLARY SEROUS CYSTADENO CARCINOMA | III |
| 103. | 1495/11 | 19 | PREGNANCY ASSOCIATED | UNILATERAL CYSTIC | BENIGN MUCINOUS CYSTADENOMA | I |
| 104. | 1667/11 | 16 | MASS ABDOMEN | UNILATERAL CYSTIC WITH PAPILLARY EXCRESCENCESS | BORDERLINE PAPILLARY SEROUS CYSTADENO FIBRMA | I |
| 105. | 1682/11 | 38 | MASS ABDOMEN | UNILATERAL CYSTIC ,PAPILLARY EXCRESCENCESS | PAPILLARY SEROUS CYSTADENOFIBROMA | I |
| 106 | 1872/11 | 26 | MASS ABDOMEN | UNILATERAL CYSTIC | BENIGN MUCINOUS CYSTADENOMA | I |
| 107. | 2082/11 | 55 | MASS ABDOMEN | UNILATERAL,CY | MUCINOUS | I |

| | | | | | | |
|---|---|---|---|---|---|---|
| | | | | STIC | CYSTADENOMA | |
| 108. | 2112/11 | 50 | MASS ABDOMEN | UNILATERAL CYSTIC | BORDERLINE MUCIONUS CYSTADENOMA | I |
| 109. | 2134/11 | 22 | PREGNANCY ASSOCIATED | UNILATERAL, CYSTIC | BENIGN MUCINOUS CYSTADENOMA | I |
| 110. | 2364/11 | 60 | ASYMPTOMATIC | UNILATERAL, CYSTIC | BENIGNSEROUS CYSTADENOMA | I |
| 111. | 2439/11 | 47 | MASS ABDOMEN | UNILATERAL, SOLID , CYSTIC, VARIEGATED | GRANULOSA CELL TUMOR | I |
| 112. | 2593/11 | 25 | MASS ABDOMEN | UNILATERAL, CYSTIC | MUCINOUS CYSTADENOMA | I |
| 113. | 2810/11 | 25 | MASS ABDOMEN | UNILATERAL, CYSTIC, PAPILLARY EXCRESCENCESS | SEROUS CYSTADNO FIBROM | I |
| 114. | 2897/11 | 38 | MASS ABDOMEN | UNILATERAL, CYSTIC | MUCINOUS CYSTADENOMA | I |
| 115. | 2985/11 | 52 | MASS ABDOMEN | UNILATERAL, SOLID | MALIGNANT SEROUS CYSTADENO CARCINOMA | III |
| 116. | 3080/11 | 35 | MASS ABDOMEN | UNILATERAL CYSTIC | MUCINOUS CYSTADENOMA | I |
| 117. | 3391/11 | 44 | MASS ABDOMEN | UNILATERAL CYSTIC | MUCINOUS CYSTADENOMA | I |
| 118. | 3427/11 | 25 | MASS ABDOMEN | UNILATERAL CYSTIC | MATURE CYSTIC TERAOMA | I |
| 119. | 3480/11 | 45 | MASS ABDOMEN | UNILATERAL SOLID | FIBROMA | I |
| 120. | 3622/11 | 21 | MASS ABDOMEN | UNILATERAL CYSTIC | MUCINOUS CYSTADENOMA | I |
| 121. | 3624/11 | 35 | MASS ABDOMEN | UNILATERAL, SOLID,CYSTIC | MUCINOUS CYSTADENO CARCINOMA | I |
| 122. | 3627/11 | 45 | MASS ABDOMEN | UNLAERAL, CYSTIC | BENIGN MUCINOUS CYSTADENOMA | I |
| 123. | 3684/11 | 25 | MASS ABDOMEN | UNILATERAL, CYSTIC | BENIGN MUCINOUS CYSTADENOMA | I |
| 124. | 3685/11 | 60 | MASS ABDOMEN | BILATERAL CYSTIC, PAPILLARY EXCRESCENCESS | B/L BORDERLINE SEROUS CYSTADENO FIBROMA | I |
| 125. | 3763/11 | 25 | MASS ABDOMEN | UNILATERAL, CYSTIC | BORDERLINE SEROUSTUMOR | I |
| 126. | 3971/11 | 42 | MASS ABDOMEN | UNILATERAL, CYSTIC | BENIGN MUCINOUS | I |

| | | | | | | |
|---|---|---|---|---|---|---|
| | | | | | CYSTADENOMA | |
| 127. | 4048/11 | 22 | ASYMPTOMATIC | UNILATERAL, CYSTIC | PAPILLARY SEROUS CYSTADENO FIBROMA | I |
| 128. | 4203/11 | 55 | ASYMPTOMATIC, | UNILATERAL, SOILD &CYSTIC | METASTATIC ADENO CARCINOMATOUS DEPOSITS | - |
| 129. | 4239/11 | 27 | MASS ABDOMEN | UNILATERAL CYSTIC | BENIGN MUCINOUS CYSTADENOMA | I |
| 130. | 4345/11 | 40 | MASS ABDOMEN | UNILATERAL CYSTIC | MATURE CYSTIC TERATOMA | I |
| 131. | 4488/11 | 45 | MASS ABDOMEN | UNILATERAL CYSTIC | BENIGN SEROUS CYSTADENOMA | I |
| 132. | 4489/11 | 27 | MASS ABDOMEN | UNILATERAL ,CYSTIC | MATURE CYSTIC TERATOMA | I |
| 133. | 4508/11 | 34 | MASS ABDOMEN | BILATERAL, CYSTIC, PAPILLARY EXCRESCENCESS | BILATERAL PAPILLARY CYSTADENO FIBROMA | I |
| 134. | 4544/111 | 25 | MASS ABDOMEN | UNILATERAL CYSTIC | MATURE CYSTIC TERATOMA | I |
| 135. | 4564/11 | 50 | MASS ABDOMEN | UNILATERAL, CYSTIC | BENIGN MUCINOUS CYSTADENOMA | I |
| 136. | 4689/11 | 45 | MASS ABDOMEN | UNILATERAL, SOLID | FIBROTHECOMA | I |
| 137. | 4758/11 | 43 | MASS ABDOMEN | BILATERAL CYSTIC | BILATERAL MATURE CYSTIC TERATOMA | I |
| 138. | 35/12 | 45 | MASS ABDOMEN | UNILATERAL CYSTIC | BENIGN SEROUS CYSTADENOMA | I |
| 139. | 48/12 | 35 | MASS ABDOMEN | UNILATERAL CYSTIC | PAPILLARY SEROUS CYTSADENO FIBROMA | I |
| 140. | 97/12 | 49 | MASS ABDOMEN | UNILATERAL CYSTIC | BENIGN SEROUS CYSTADENO FIBROMA | I |
| 141. | 343/12 | 50 | MASS ABDOMEN,ASCITES | BILATERAL SOLID,CYSTIC | B/L SEROUS CYSTADENO CARCINOMA | III |
| 142. | 800/12 | 25 | MAS S ABDOMEN | UNILATERAL, CYSTIC | BENIGN MUCINOUS CYSTADENOMA | I |
| 143. | 921/12 | 45 | MASS ABDOMEN | BILATERAL, SOLID | BILATERAL KRUKENBERG | |
| 144. | 1131/12 | 55 | MASS ABDOMEN | UNILATERAL, SOLID AND | BENIGN MUCINOUS AND | I |

| | | | | | | |
|---|---|---|---|---|---|---|
| | | | | CYSTIC | BENIGN BRENNER | |
| 145. | 1371/12 | 45 | MASS ABDOMEN | UNILATERAL, CYSTIC | MUCINOUS CYSTADENOMA | I |
| 146. | 1376/12 | 55 | ASYMPTOMATIC | UNILATERAL, SOLID | BENIGN BRENNER TUMOR | I |
| 147. | 1693/12 | 32 | MASS ABDOMEN | UNILATERAL, CYSTIC ,FOCAL SOLID | BORDERLINE MUCINOUS CYSTADENOMA | I |
| 148. | 1869/12 | 16 | MASS ABDOMEN | UNILATERAL CYSTIC | BENIGN MUCINOUS CYSTADENOMA | I |
| 149. | 1870/12 | 58 | MASS ABDOMEN | UNILATERAL CYSTIC | BORDERLINE MUCINOUS CYSTADENOMA | I |
| 150. | 2121/12 | 20 | PAIN & MASS ABDOMEN | UNILATERAL, SOLID | DYSGERMINOMA | I |

# OBSERRVATION AND RESULTS

# OBSERVATION AND RESULTS

Thisprospective study covered a total number of 150 ovarian neoplasms referred from Raja Mirasudhar Government hospital(RMH),Thanjavur Medical college during the study period from 2010 to May 2012.

We received bilateral,unilateral salphingo-oophorectomy along with total abdominal hysterectomy and ovariatomy specimens. Specimens were fixed in to in neutral buffered formalin and processed routinely.

**I: INCIDENCE:**

The following table (table 3) shows the total number of ovarian neoplasms among female neoplasms.

**TABLE 3: TOTAL NUMBER OF OVARIAN NEOPLASMS IN RELATION TO TOTAL FEMALE NEOPLASMS.**

| SL.NO | PERIOD | TOTAL NO OF FEMALE NEOPLASMS | TOTAL NO OF OVARIAN NEOPLASMS | % |
|---|---|---|---|---|
| 1. | Jan10-May10 | 396 | 32 | 8.08% |
| 2. | Jun10-Dec10 | 424 | 36 | 8.4% |
| 3. | Jan11-May11 | 389 | 26 | 6.6% |
| 4. | May11-Dec11 | 422 | 33 | 7.8% |
| 5. | Jan12-May12 | 289 | 23 | 7.9% |
| | Total | 1920 | 150 | 7.8% |

The average incidence of ovarian neoplasms(including benign and malignant) among females is 7.8%. [CHART 1].

## II. AGE INCIDENCE :

In this study ovarian neoplasms were in the age group ranging from 10 to 79 years. The patients were divided into 7 groups according to their age(i.e, 10-19 yrs,20-29 yrs,30-39 yrs,40-49 yrs, 50-59 yrs,60-69 yrs and 70-79 yrs), Age incidence of ovarian neoplasms is shown in the following Table 4.

**TABLE 4: AGE INCIDENCE OF OVARIAN NEOPLASMS**

| SL.NO | AGE IN YEARS | TOTAL NO.OF CASES | % |
|---|---|---|---|
| 1 | 10-19 | 5 | 3.3 % |
| 2 | 20-29 | 44 | 29.3 % |
| 3 | 30-39 | 29 | 19.3 % |
| 4 | 40-49 | 37 | 24.6 % |
| 5 | 50-59 | 25 | 16.6 % |
| 6 | 60-69 | 8 | 5.3 % |
| 7 | 70-79 | 2 | 1.3 % |
| | TOTAL | 150 | |

From the above table it is evident that the highest incidence of ovarian neoplasms is seen in the age group between 20-29 yrs and the lowest

incidence is after 70 yrs of age.[CHART2]

**CHART 1: COMPARISON OF OVARIAN NEOPLASMS IN RELATION TO TOTAL OVARIAN NEOPLASMS**

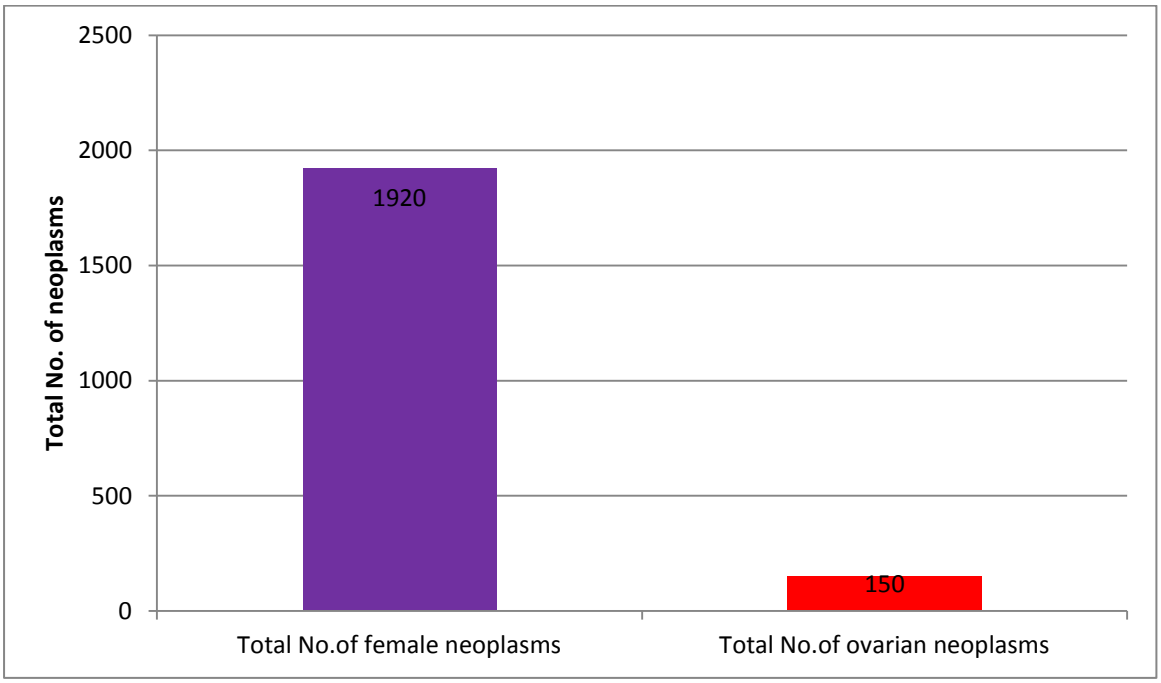
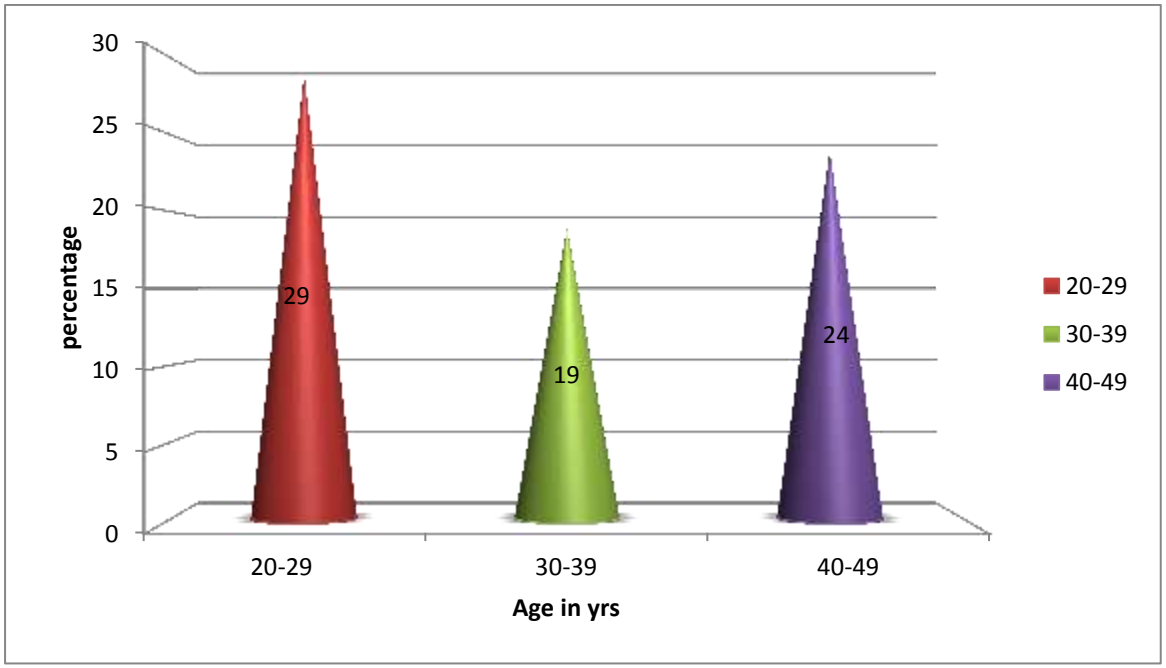



**CHART 2: AGE INCIDENCE OF OVARIAN NEOPLASMS**



## III. AGE INCIDENCE OF CATEGORIES OF OVARIAN NEOPLASMS :

The ovarian neoplasms are divided into Benign, Borderline, Malignant categories as given in the following table.5

**TABLE 5:**

| SL.NO | AGE – YEARS | BENIGN | BORDERLINE | MALIGNANT |
|---|---|---|---|---|
| 1 | 10-19 | 3 | 1 | 1 |
| 2 | 20-29 | 40 | 1 | 3 |
| 3 | 30-39 | 19 | 2 | 8 |
| 4 | 40-49 | 28 | 3 | 6 |
| 5 | 50-59 | 11 | 3 | 11 |
| 6 | 60-69 | 5 | 2 | 1 |
| 7 | 70-79 | 1 | - | 1 |
| | TOTAL | 109 (72.6%) | 12 (8%) | 29 (19.3%) |

From the above table.5, it is evident that the highest incidence of benign neoplasms is seen in 20-29 yrs(40/109 cases,37%), borderline neoplasm in 40-49 yrs (3/109 cases,25%) and malignant neoplasm in 50-59 yrs ( 11 /29cases, 52%). [CHART 3]

**CHART 3: AGE INCIDENCE OF CATEGORIES OF OVARIAN NEOPLASMS**

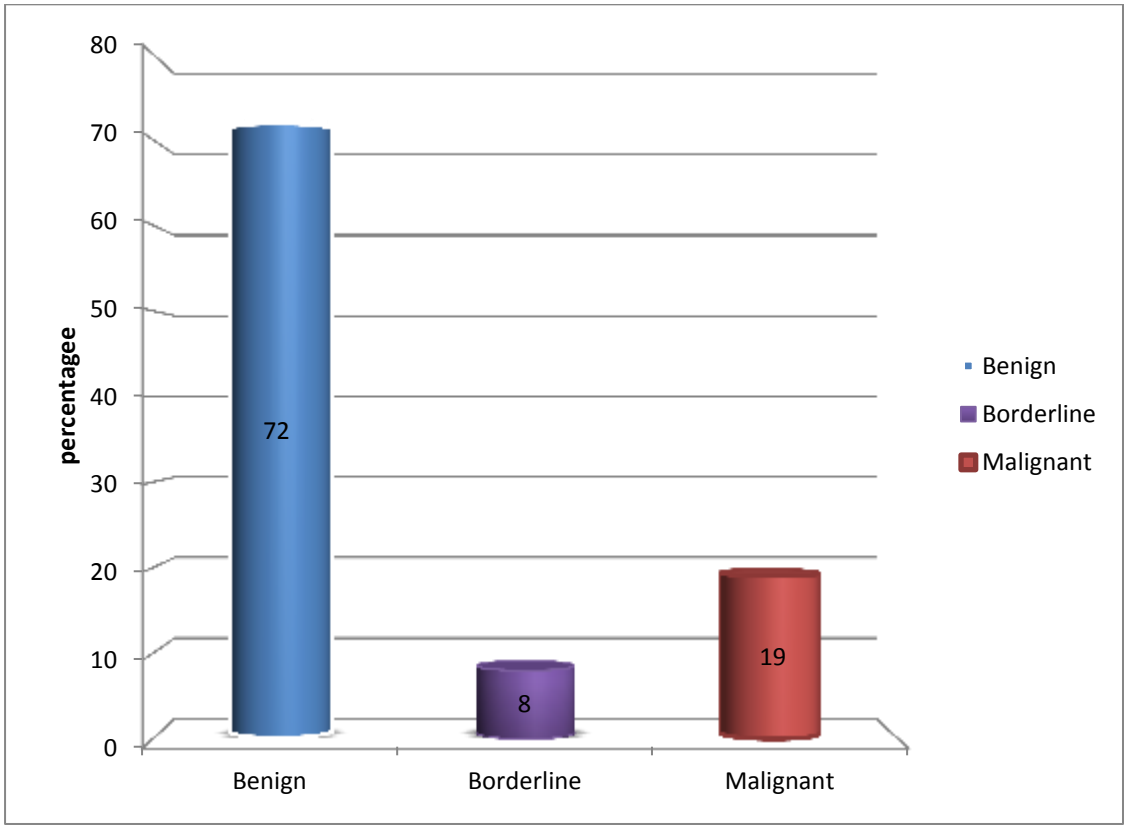


**TABLE 5A: FREQUENCY DISTRIBUTION OF INDIVIDUAL BENIGN TUMORS IN DIFFERENT AGE GROUPS.**

| Diagnosis | Age 10-19 yrs | Age 20-29 yrs | Age 30-39 yrs | Age 40-49 yrs | Age 50-59 yrs | >60 Yrs | Total(%) |
|---|---|---|---|---|---|---|---|
| Serous cystadenoma | - | 11 | 5 | 8 | 2 | 2 | 28 (25.6%) |
| Serous cystadenofibroma | - | 4 | 5 | 7 | 2 | 2 | 20 (18.3%) |
| Mucinous cystadenoma | 1 | 9 | 10 | 10 | 1 | 1 | 32 (29.3%) |
| Benign Brenner | - | - | - | 1 | 2 | - | 3 (2.75%) |
| Fibroma | - | 1 | - | 1 | - | 1 | 3 (2.75%) |
| Mature cystic teratoma | - | 10 | 4 | 5 | 3 | - | 22 (20.1%) |
| Fibrothecoma | - | - | - | 1 | - | - | 1 (0.9%) |
| Total | 1 | 35 | 24 | 33 | 10 | 6 | 109 (100%) |

**TABLE 5B: FREQUENCY DISTRIBUTION OF INDIVIDUAL MALIGNANT TUMORS IN DIFFERENT AGE GROUPS**

| Diagnosis | Age 10-19 yrs | Age 20-29 yrs | Age 30-39 yrs | Age 40-49 yrs | Age 50-59 yrs | Age >60 yrs. | Total% |
|---|---|---|---|---|---|---|---|
| Papillary Serous cystadenocarcinoma | - | - | 1 | 2 | 5 | 2 | 10(34.4%) |
| Mucinous cystadenocarcinoma | - | 1 | 2 | - | 1 | - | 4(13.6%) |
| Granulosa cell tumor | - | 1 | 2 | 3 | 3 | - | 9(31.2%) |
| Dysgerminoma | - | 1 | - | - | - | - | 1(3.4%) |
| Mixed germ cell tumor | 1 | - | - | - | - | - | 1(3.4%) |
| Metastatic adeno/krukenberg | - | - | 1 | 1 | 2 | - | 4(13.6%) |
| Total | 1 | 3 | 6 | 6 | 11 | 2 | 29(100%) |

Of all patients with serous carcinomas(figure2) 50 %(5/10 cases)

patients were in the age group of 50-59 yrs, 20 %(2/10 cases) were in the agegroup of 40-49 and 60-69 yrs. 4 patients had mucinous cystadenocarcinoma (figure 3)among which 50 % (2/4 cases) are in30-39 yrs and Metastatic tumors predominates after the age of 50 yrs.

## IV. CLINICAL EVALUATION:

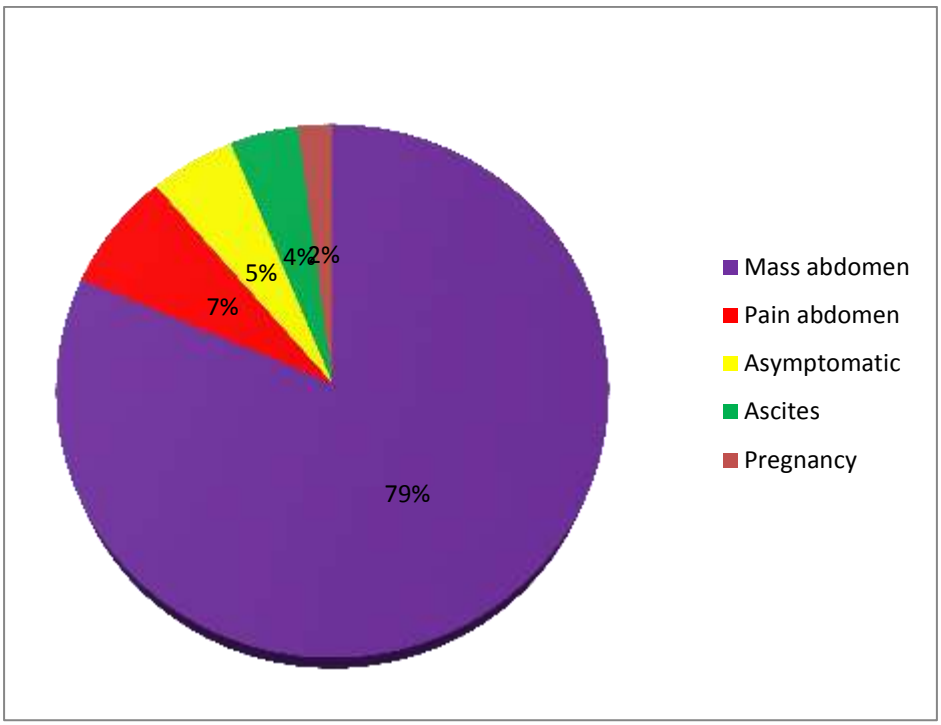
All the cases were evaluated clinically at the time of admission as in the following table 6.

**TABLE 6: CLINICAL FEATURES OF VARIOUS OVARIAN TUMORS**

| SL.NO | CLINICAL FEATURES | NO.OF CASES | % |
|---|---|---|---|
| 1. | Mass abdomen | 119 | 79.3 % |
| 2. | Pain abdomen | 11 | 7.3 % |
| 3. | Pregnancy associated | 4 | 2.6 % |
| 4. | Ascites | 7 | 4.6 % |
| 5. | Asymptomatic | 9 | 6 % |

Abdominal mass is the most common clinical Presentation (119 cases,79.3%) followed by abdominal pain(11 cases,7.3%) Four cases were found to be associated with pregnancy. Nine cases were asymptomatic and detected during abdominal ultrasonography done for other causes(CHART 4)

**CHART 4: PIE CHART DEPICTING THE PERCENTAGE OF SIGNS ANDSYMPTOMS AMONG OVARIAN TUMOR PATIENTS.**



**V. LATERALITY:**

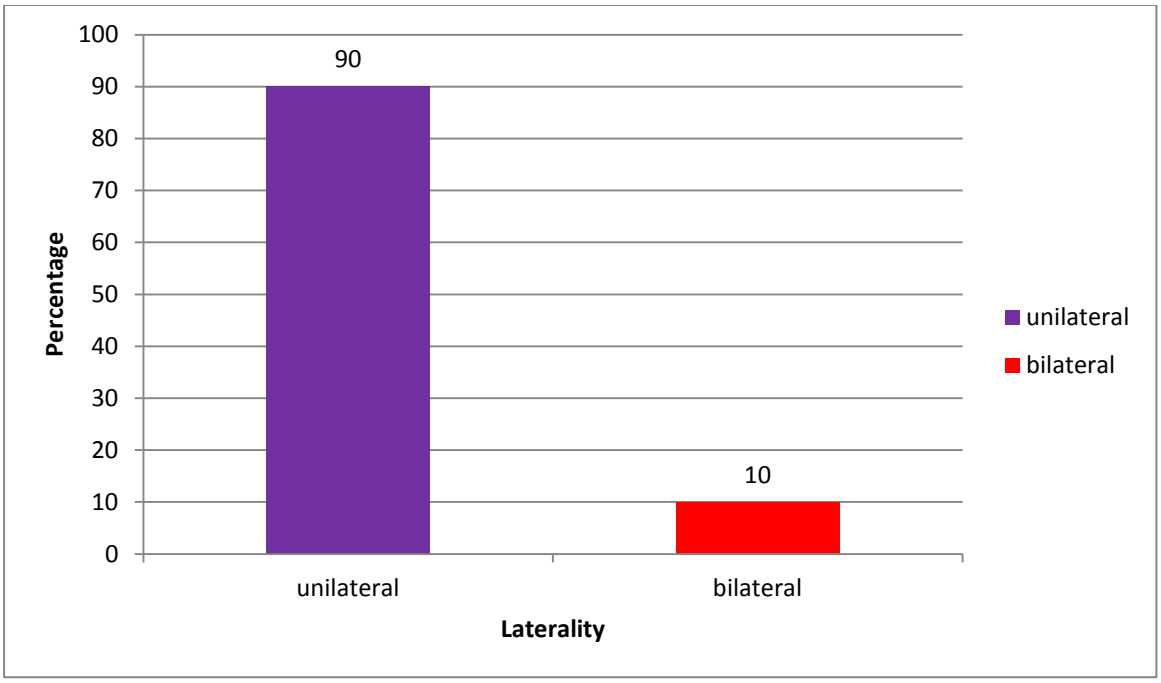
Likewise tumors are also categorised as with unilateral/bilateral ovarian involvement as in the given table.7 .

**TABLE 7: DISTRIBUTION OF OVARIAN TUMORS IN RELATION TO LATERALITY OF INVOLVEMENT.**

| L.NO | TUMORS | UNILATERAL | % | BILATERAL | % |
|---|---|---|---|---|---|
| 1. | SEROUS<br>Benign<br>Borderline<br>Malignant | <br>44<br>2<br>6 | | <br>4<br>1<br>4 | |
| | TOTAL | 52 | 38.2% | 9 | 65% |
| 2 | MUCINOUS<br>Benign<br>Borderline<br>Malignant | <br>31<br>9<br>4 | | <br>1<br>-<br>- | |
| | TOTAL | 44 | 32.3% | 1 | 7% |
| 3. | TRANSITIONAL | 3 | | - | |
| 4. | SEXCORD-STROMAL | 13 | | - | |
| 5. | GERM CELL TUMOR | 23 | 23% | 1 | 7% |
| 6. | METASTATIC | 1 | | - | |
| 7. | KRUKENBERG | | | 3 | 21% |
| | Grand Total | 136 | | 14 | |

The above table .7, shows that among serous tumors 52/61 cases,(85

**CHART 5: DISTRIBUTION OF OVARIAN TUMORS IN RELATION TO LATERALITY OF INVOLVEMENT**



% ) were unilateral at the time of presentation and 9/61,( 14.7%) cases were bilateral. Among mucinous tumors (figure 4,10,11),44/45 cases,(97.7 % ) were unilateral and 1/45(2.2%) cases were bilateral. Among germ cell tumors, 23/24 cases(98.9 %) were unilateral and 1/24 (4.1%) cases were bilateral. Most of the Metastatic tumors(fig.6,18,19) ,3/4 cases,(75 %) were bilateral at the time of presentation.

Bilateral ovarian tumors were seen in 14 cases. Bilaterality was more a feature of malignant tumors. 31% (9/29) of malignant tumors were bilateral whereas only 4.5%(5/109) benign tumors were bilateral. Among malignant tumors 50% serous carcinomas(figure8,9) are bilateral followed by metastatic tumors (75%.) None of the mucinous cystadenocarcinomas (figure25)were bilateral. (CHART5)

**VI. GROSS MORPHOLOGY OF OVARIAN NEOPLASMS :**

The ovarian neoplasms were divided into following types according to gross morphology as shown in following table.8.

**CHART 6: GROSS MORPHOLOGY OF OVARIAN TUMORS**

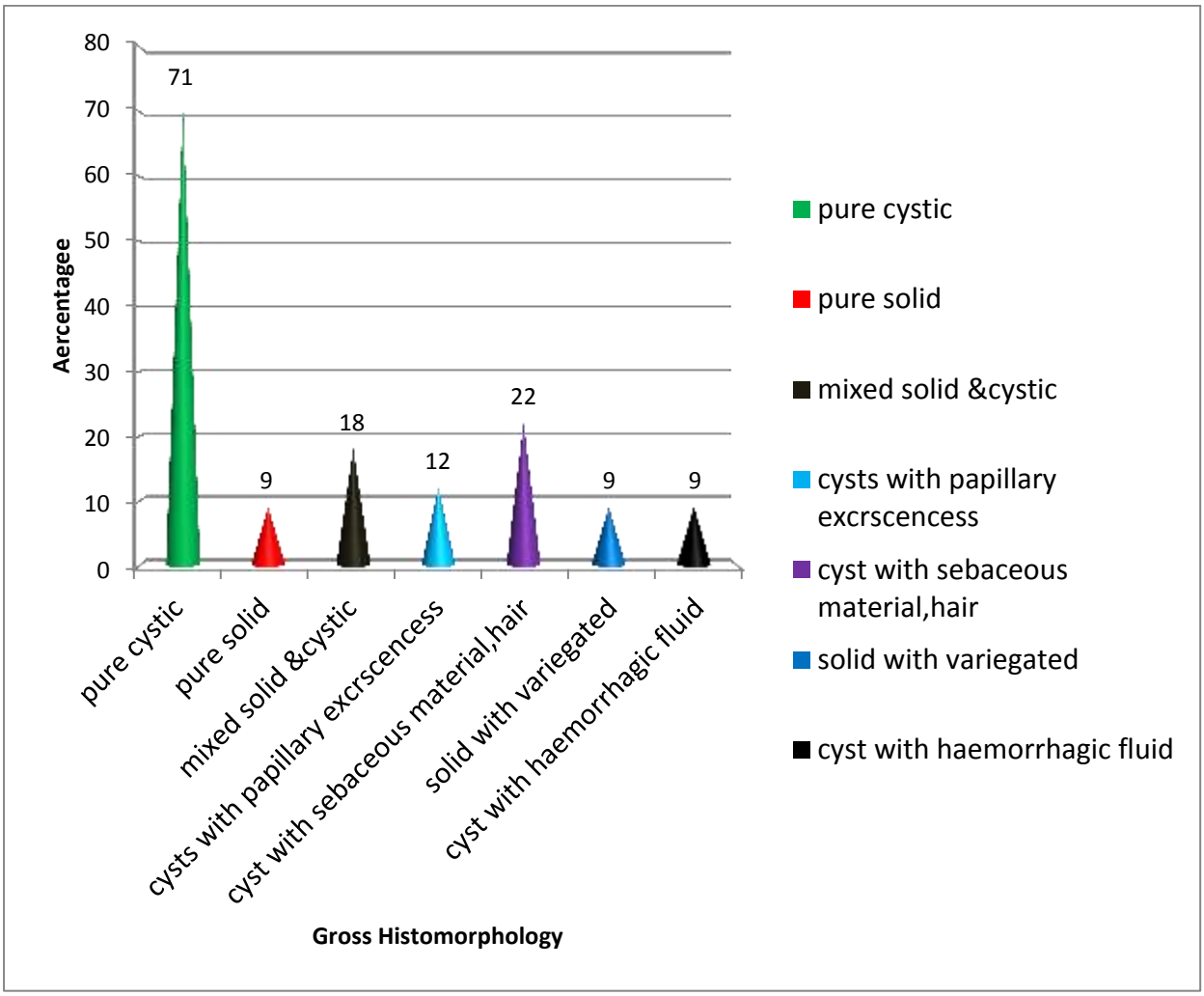


**TABLE 8:GROSS MORPHOLOGY OF OVARAIN NEOPLASMS:**

| SL.NO | GROSS MORPHOLOGY | NUMBER OF CASES(%) |
|---|---|---|
| 1. | Pure solid | 9 (6%) |
| 2. | Pure cystic | 71 (47.3%) |
| 3. | Mixed solid & cystic | 18 (12%) |
| 4. | Cystic with papillary excrescencess | 12(8%) |
| 5. | Solid with variegated appearance | 9(6%) |
| 6. | Cysts with haemorrhagic fluid | 9(6%) |
| 7. | Cyst with sebaceous material&hair. | 22(14%) |
| | TOTAL | 150 (100%) |

Most common presentation of ovarian tumors in this study as shown in the above table.8. is purely cystic masses ( 71 cases,47%). Followed by cysts with sebaceous material and hair(22 cases, 14%) and Mixed solid and cystic tumors( 18 cases,12%). Least common presentation is purely solid tumors(6%). [CHART6].

**VII : DISTRIBUTION OF OVARIAN NEOPLASMS ACCORDING TO HISTOLOGICAL CLASSIFICATION.TABLE 9:**

| SL.NO | CLASSIFICATION | NO.OF CASES | TOTAL CASES | % |
|---|---|---|---|---|
| 1. | SURFACE EPITHELIAL TUMOR<br>Benign<br>Borderline<br>Malignant | <br>83<br>12<br>14 | 109 | 72.6% |
| 2. | GERM CELL TUMOR<br>Benign<br>Malignant | <br>22<br>2 | 24 | 16% |
| 3. | SEXCORD-STROMAL TUMOR<br>Benign<br>Malignant | <br>4<br>9 | 13 | 8.6% |
| 4. | METASTATIC | 4 | 4 | 2.6% |
| | Total | 150 | 150 | |

It is evident from the above table .9. that ,of the total 150 neoplasms , surface epithelial tumors predominates with 109 cases(72.6%),followed by germ cell tumors with 24 cases(16%) and sex cord – stromal tumors (13 cases,8.6%).[CHART7].

**CHART 7: INCIDENCE OF HISTOLOGICAL TYPES OF OVARIAN NEOPLASMS IN RELATION TO TOTAL OVARIAN NEOPLASMS**

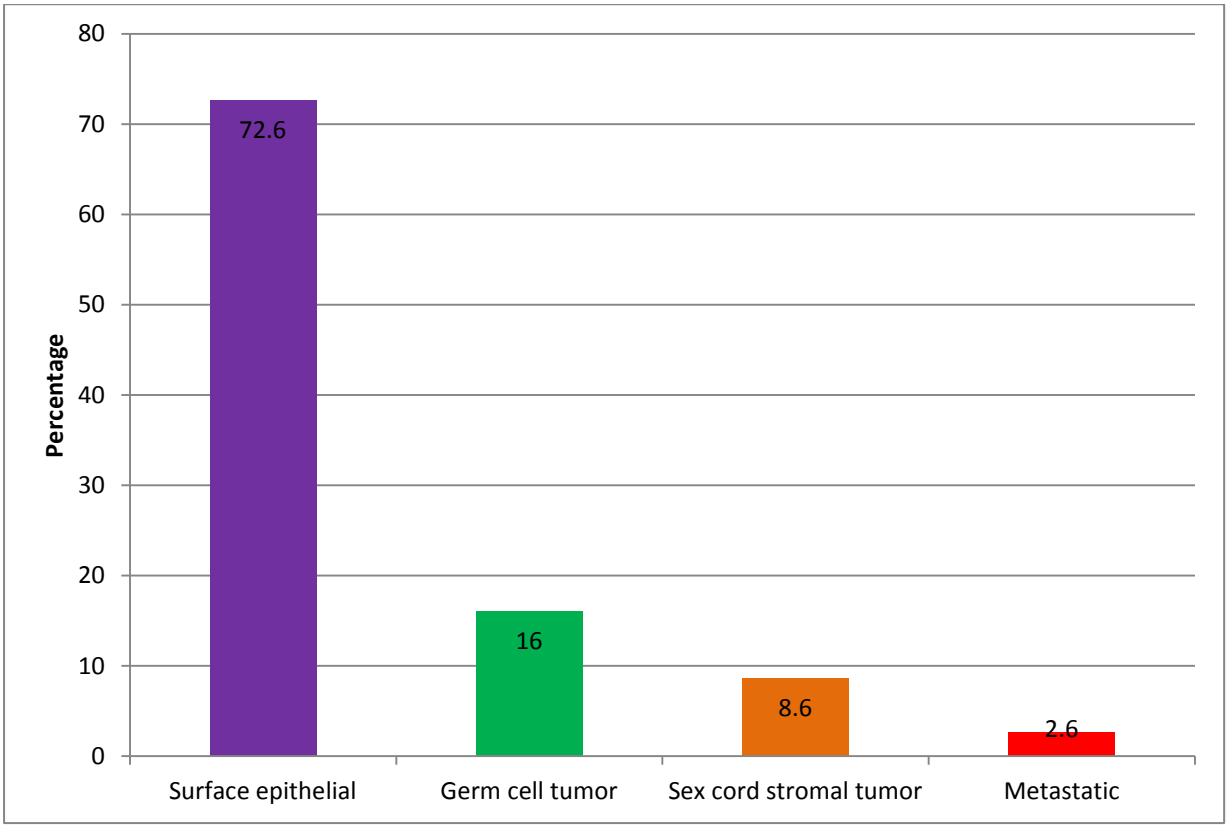
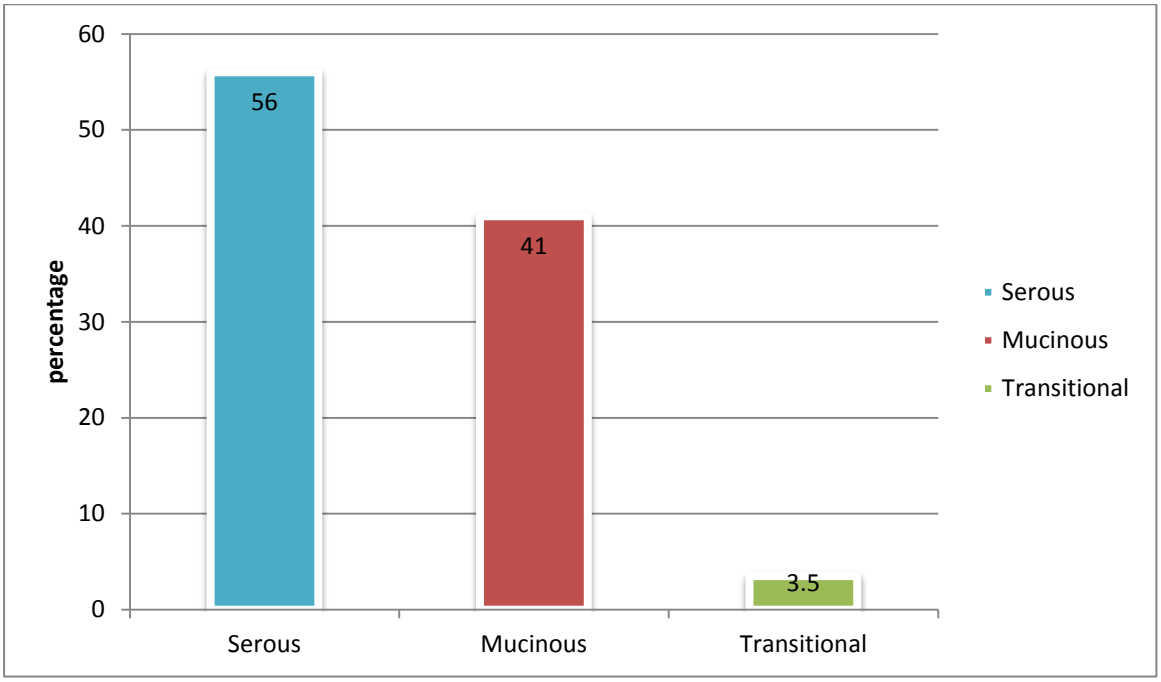


**CHART 8: INCIDENCE OF HISTILOGICAL SUBTYPES OF SURFACE EPITHELIAL TUMORS**



## III:SUBCLASSIFICATION OF SURFACE EPITHELIAL TUMORS:

Surfac epithelial tumors are classified according to WHO HISTOLOGICAL CLASSIFICATION and is given in the following table 10.

**TABLE 10:**

| SL.NO | CLASSIFICATION | NO.OF CASES | % | AVERAGE |
|---|---|---|---|---|
| 1. | SEROUS TUMORS | | | |
| | Benign | 48 | 78.6 % | |
| | Borderline | 3 | 4.9% | 55.9% |
| | Malignant | 10 | 16.3 % | |
| | TOTAL | 61 | | |
| 2. | MUCINOUS | | | |
| | Benign | 32 | 71.1 % | |
| | Borderline | 9 | 20 % | 41.2% |
| | Malignant | 4 | 8.8 % | |
| | TOTAL | 45 | | |
| 3. | TRANSITIONAL | | | |
| | Benign Brenner | 3 | 3% | 3.3% |
| | Grand total | 109 | | |

From the above table.10, it is evident that among all surface epithelial tumors, Serous tumors predominates (61cases,55.9 %) followed by mucinous tumors (45cases, 41 %) and 3 cases of transitional tumor (figure4,12) were also observed.[CHART8].

**IX : HISTOMORPHOLOGICAL FEATURES OF BORDERLINE SURFACE EPITHELIAL TUMORS:TABLE 11:**

| SL.NO | HISTOLOGICAL FEATURE | NO.OF CASES |
|---|---|---|
| 1.SEROUS BORDERLINE | Histology:<br>1.Typical<br>2.Micropapillary | <br>3<br>0 |
| | Laterality:<br>1.Unilateral<br>2.Bilateral | <br>2<br>1 |
| | Surface involvement<br>1.Present<br>2. Absent | <br>0<br>3 |
| | Microinvasion<br>1.Present<br>2.Absent | <br>0<br>3 |
| 2.MUCINOUS BORDERLINE | Histology:<br>1.Intestinal<br>2.Endocervical | <br>9<br>0 |

The above table. 11, shows that all cases of borderline serous tumors(figure1,7,22) showed a typical hierrarchial branching pattern of papillae (3cases,100%) . At the time of presentation ,2 cases were unilateral and 1 case was bilateral. None of the three cases showed surface involvement nor microinvasion. Table also shows that all mucinous borderline tumors (figure24) , 4/4 cases,(100%) were of Intestinal type.

**X: HISTOMORPHOLOGY OF MALIGNANT SURFACE EPITHELIAL TUMOR:TABLE 12:**

| SL.NO | HISTOLOGICAL TYPE | NO.OF CASES |
|---|---|---|
| 1. | SEROUS-GRADING<br>1.LOW GRADE<br>2.HIGH GRADE | <br>4<br>6 |
| | TOTAL | 10 |
| 2. | MUCINOUS<br>TYPE OF INVASION<br>1.EXPANSILE<br>2.INFILTRATING | <br><br>4<br>0 |
| | TOTAL | 4 |

Malignant serous tumors are graded according to recent 2-tier system of classification. Above table. 12, shows that , 4/10 cases(40%) were low grade carcinomas and 6/10 cases(60%) were high grade. High grade serous carcinomas are common among all serous carcinomas. All 4 cases of mucinous carcinomas showed expansile type of invasion.

**XI.SEX CORD STROMAL CELL TUMORS:**

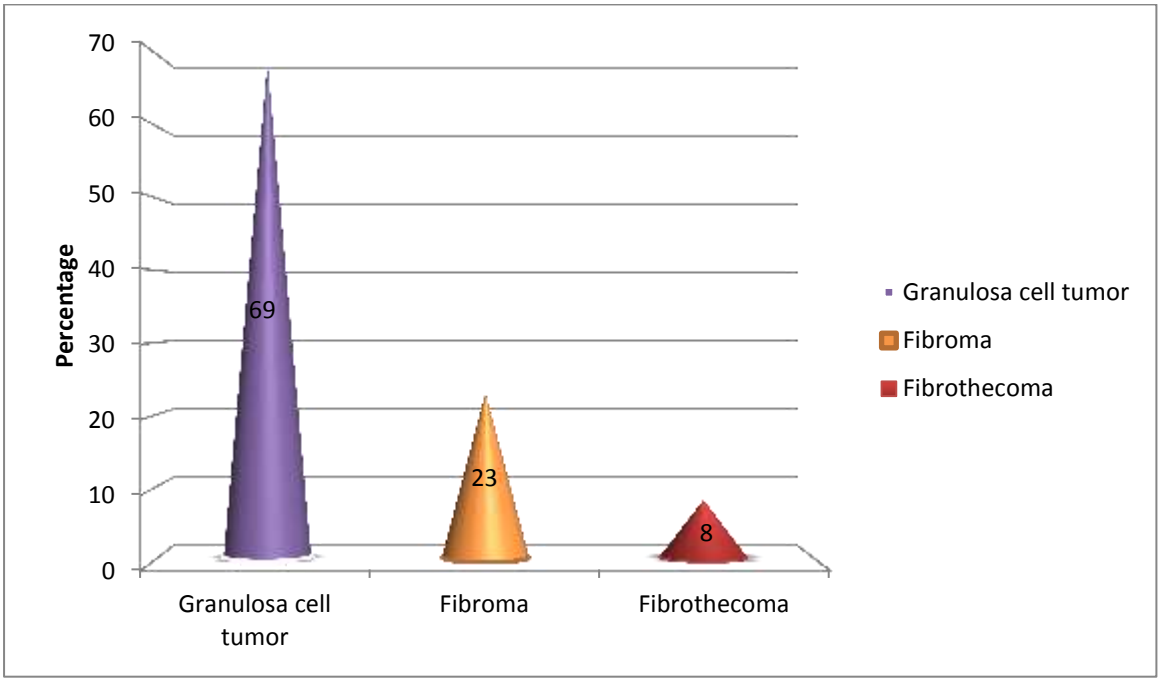
Sex cord –stromal tumors were sub-classified and their individual incidence is given in the following table .13.

**TABLE 13:**

| SL.NO | CLASSIFICATION | NO.OF CASES | % |
|---|---|---|---|
| 1. | Granulosa cell tumor<br>1.adult type<br>2. juvenile type | <br>9<br>0 | <br>69 % |
| 2. | Fibroma | 3 | 23 % |
| 3. | Fibrothecoma | 1 | 8 % |
| | Total | 13 | |

The above table.13, shows that,among sex cord stromal cell tumors group , granulosa cell tumor (figure13) predominates( 9 cases, 69%) followed by fibroma (figure15) (3cases,23%) and fibrothecoma(figure14) (1 case,8%). [CHART 9]

**CHART 9: INCIDENCE OF SUBTYPES OF SEX CORD- STROMAL TUMORS**



## XII : GERM CELL TUMORS:

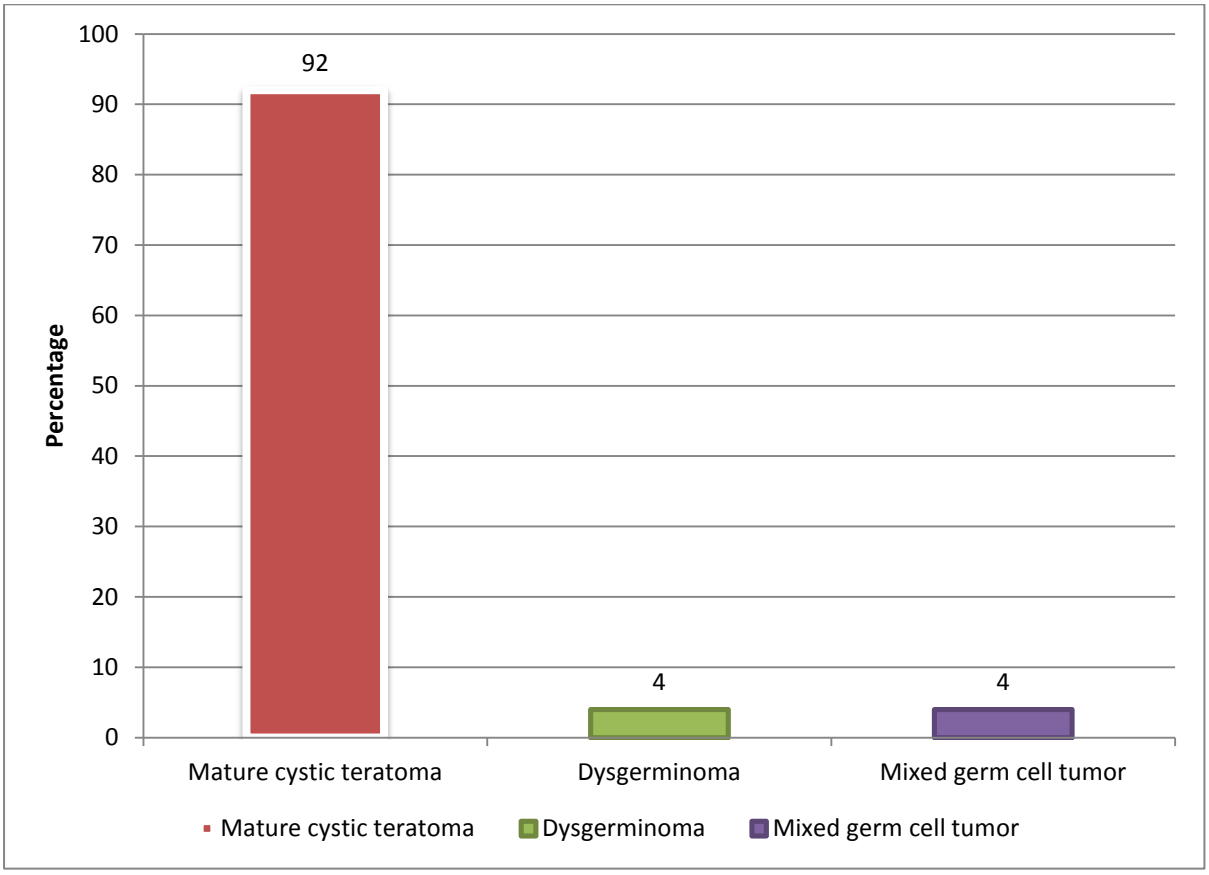
Germ cell tumors were subclassified and their individual tumor incidence is given in the following table.14

**TABLE 14:**

| SL.NO | CLASSIFICATION | NO.OF CASES | % |
|---|---|---|---|
| 1. | Teratoma<br>1.Benign<br>2.Malignant | 22 | 91.6% |
| 2. | Dysgerminoma | 1 | 4.1% |
| 3. | Mixed germ cell tumor | 1 | 4.1% |
| | Total | 24 | |

From the above table .14, it is evident that among Germ cell tumor group, Mature cystic teratomas predominates( 22 cases,91%) followed by Dysgerminoma (figure5,16) ( 1 case,4%) and Mixed germ cell tumor (figure17) (1 case, 4%).CHART10.

**CHART 10: INCIDENCE OF SUBTYPES OF GERM CELL TUMORS**



## XIII: IMMUNOHISTOCHEMISTRY: KI-67 LABELLING INDEX

**TABLE 15:A**

| SL.NO | HPE.NO | HPE.DIAGNOSIS | Ki-67(LI) |
|---|---|---|---|
| 1. | 1667/11 | Borderline serous tumor | 24% |
| 2. | 3685/11 | Borderline serous tumor | 19% |
| 3. | 3763/11 | Borderline serous tumor | 26% |
| 4. | 1096/10 | Borderline mucinous tumor | 28% |
| 5. | 1314/10 | Borderline mucinous tumor | 24% |
| 6. | 2151/10 | Borderline mucinous tumor | 26% |
| 7. | 2499/10 | Borderline mucinous tumor | 30% |
| 8. | 2799/10 | Borderline mucinous tumor | 18% |
| 9. | 294/11 | Borderline mucinous tumor | 23% |
| 10. | 2112/11 | Borderline mucinous tumor | 29% |
| 11. | 1693/12 | Borderline mucinous tumor | 31% |
| 12. | 1870/12 | Borderline mucinous tumor | 23% |
| 13. | 442/10 | High grade serous Carcinoma | 52% |
| 14. | 1809/10 | High grade serous Carcinoma | 47% |
| 15. | 2438/10 | High grade serous Carcinoma | 44% |
| 16. | 3136/10 | Low grade serous Carcinoma | 43% |
| 17. | 3257/10 | Low grade serous Carcinoma | 39% |
| 18. | 3529/10 | High grade serous Carcinoma | 42% |

| | | | |
|---|---|---|---|
| 19. | 181/11 | Low grade serous Carcinoma | 33% |
| 20. | 1481/11 | High grade serous Carcinoma | 46% |
| 21. | 2985/11 | Low grade serous Carcinoma | 41% |
| 22. | 343/12 | High grade serous Carcinoma | 48% |
| 23. | 2605/10 | Mucinous Carcinoma | 38% |
| 24. | 4275/10 | Mucinous carcinoma | 36% |
| 25. | 760/11 | Mucinous carcinoma | 42% |
| 26. | 3624/11 | Mucinous carcinoma | 40% |

ki-67 labelling index was done in all 12 cases of borderline tumors and 14 cases of malignant tumors of epithelial origin. Diffuse intense nuclear staining is considered as positive and weak cytoplasmic staining is considered as negative.

**TABLE 15 B: p53 IMMUNOHISTOCHEMISTRY**

| SL.NO | HPE NO | HPE DIAGNOSIS | p53 IHC |
|---|---|---|---|
| 1. | 442/10 | High grade serous Carcinoma | Positive |
| 2. | 1809/10 | High grade serous Carcinoma | Positive |
| 3. | 2438/10 | High grade serous Carcinoma | Positive |
| 4. | 3136/10 | Low grade serous Carcinoma | Positive |
| 5. | 3257/10 | Low grade serous Carcinoma | Positive |
| 6. | 3529/10 | High grade serous Carcinoma | Positive |
| 7. | 181/11 | Low grade serous Carcinoma | Negative |
| 8. | 1481/11 | High grade serous Carcinoma | Negative |
| 9. | 2985/11 | Low grade serous Carcinoma | Positive |
| 10. | 343/12 | High grade serous Carcinoma | Negative |
| 11. | 2605/10 | Mucinous Carcinoma | Negative |
| 12. | 4275/10 | Mucinous carcinoma | Negative |
| 13. | 760/11 | Mucinous carcinoma | Negative |
| 14. | 3624/11 | Mucinous carcinoma | Negative |

P53 immunohistochemical staining was applied to all (14) cases of malignant tumors of surface epithelial origin like serous carcinomas including low and high grade and mucinous carcinomas. Results were interpreted as Positive when cells shows diffuse and intense nuclear staining.

**XIV: P53 EXPRESSION IN TYPE I AND TYPE II SURFACE EPITHELIAL TUMORS OVARY:TABLE 16:**

| Type of ovarian tumor | | P53expression Positive | P53expression Negative | Total |
|---|---|---|---|---|
| TypeI | Low grade serous Carcinoma | 1(25%) | 3(75%) | 4 |
| Type II | High grade serous carcinoma | 5(83.3%) | 1(16.7%) | 6 |

The above table.16 shows that about 3 cases(75%) of low grade serous carcinoma belonging to type I pathway of tumorigenesis, showed negative for p53 immunohistochemical staining (figure 21). Whereasabout 5 cases (83%) of high grade serous carcinoma which are included in the type II pathway of tumorigenesis showed positivity for p53 staining. (figure 20)

**XV: Ki -67 EXPRESSION IN SEROUS TUMORS:TABLE 17:**

| Sl.no | HPE DIAGNOSIS | 0-25 | 26-50 | 51-75 | 76-100 | Total |
|---|---|---|---|---|---|---|
| 1. | Serous Borderline | 2(66.7%) | 1(33.3%) | - | - | 3 |
| 2. | Serous Malignant | - | 9(90%) | 1(10%) | - | 10 |

There are three serous borderline tumors in total. From the above table. 17 it is evident that each one of them had a different level of expression of ki-67 labelling index. One case showed a ki-67 LI of 24%, second tumorshowed ki-67 LI of 19%(figure 22), and the third case showed a ki-67 LI of26% and

this was found to be the greatest level of expression among all serous borderline tumors.

The above table.17 also shows that there are about 10 cases of serous carcinomas(figure23) of which 9 cases showed ki-67 LI between 26-50 and 1 case showed ki-67 LI above 50. Highest level of ki-67 LI was found to be in high grade serous carcinomas. Among all high grade(6/10) serous carcinoma, highest ki-67 LI was found to be 52% and lowest value among high grade tumors was 42%. Among the four low grade tumors highest ki-67 expression was 43% and the least value was found to be 39%.

**XVI: KI-67 EXPRESSION IN MUCINOUS TUMORSTABLE 18:**

| Sl.no | HPE Diagnosis | 0-25 | 26-50 | 51-75 | 76-100 | Total |
|---|---|---|---|---|---|---|
| 1. | Mucinous Borderline | 4(44.4%) | 5(55.5%) | - | - | 9 |
| 2. | Mucinous carcinoma | - | 4 | - | - | 4 |

There were about nine mucinous borderline tumors (figure24). The above table.18 shows that ki-67 LI in 4 cases , 44% of mucinous borderline tumors was between 0-25 and 5 cases ,55% showed ki-67 LI between 26-50. Among them highest level of ki-67 expression found was 30% and the least ki-67 LI was 23%. The above table.18 also shows that there were about 4 cases of

mucinous carcinomas (figure 25), all 4 showed ki-67 LI was between 26-50. Of them the highest level of Ki-67was 40% and least value was 36%.

The immunostaining pattern was heterogenous throughout the tumor and evaluation was done in most positively stained areas.The mean ki-67 LI in borderline tumors was 25% (19-31%). Mean ki-67 LI in malignant tumors was 42% (33-52%). When compared with the borderline tumors ,ki-67 LI was found to be statistically significant increase in malignant tumors($p<0.005$).In malignant group of tumors, Serous carcinomas(figure23) showed high index of 52%, followed by Mucinous carcinomas (figure 25) with a mean index of 39%.


FIGURE 1 : BILATERAL BORDERLINE SEROUS CYSTADENOMA. CUT SURFACE- MULTILOCULATED CYSTS WITH NUMEROUS TINY PAPILLARY EXCRESCENSESS .


FIGURE 2: BILATERAL PAPILLARY SEROUS CYSTADENOCARCINOMA WITH SOLID AND CYSTIC AREAS WITH OMENTAL DEPOSITS(ARROW).


FIGURE 3 : MUCINOUS CYSTADENOCARCINOMA. CUT SURFACE- SHOWS MULTILOCULATED CYST FILLED WITH MUCIN AND FOCAL SOLID AREAS.


FIGURE 4: MUCINOUS CYSTADENOMA WITH BRENNER TUMOR.CUT SURFACE-MULTILOCULATED CYSTS FILLED WITH MUCIN AND FOCAL YELLOW SOLID AREA MEASURING 2X2CM.(BRENNER).

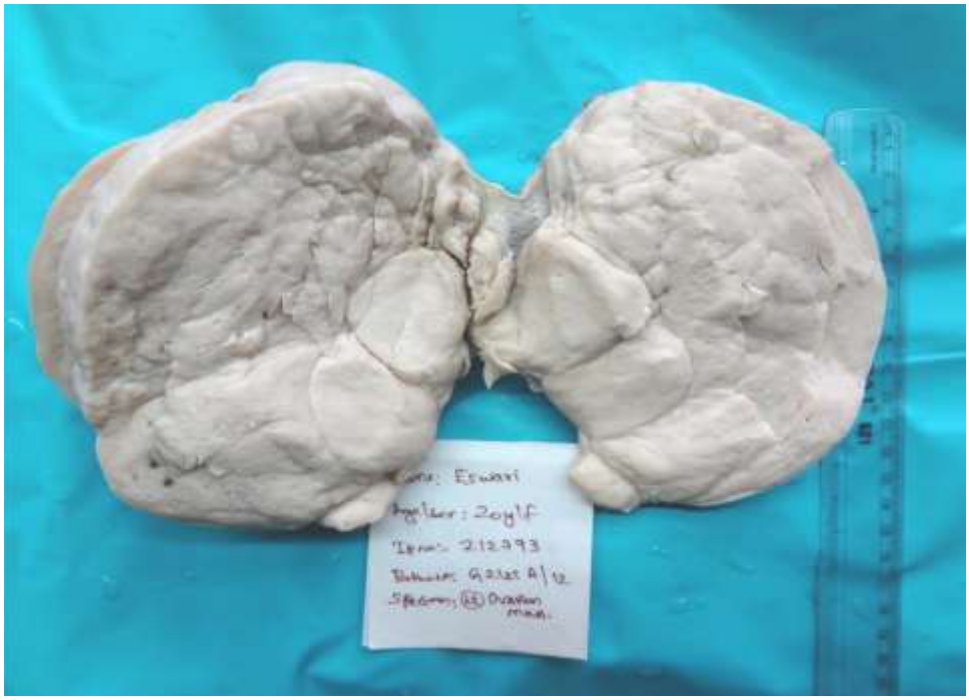


FIGURE 5 : DYSGERMINOMA.CUT SURFACE SHOWS SOLID HOMOGENOUS,FIRM,LOBULATED GREY TAN MASS.


FIGURE 6: KRUKENBERG TUMOR.TYPICALLY INVOLOVEMENT IS BILATERAL& ARE CHARACTERISED BY MULTINODULAR EXTERNAL SURFACE.

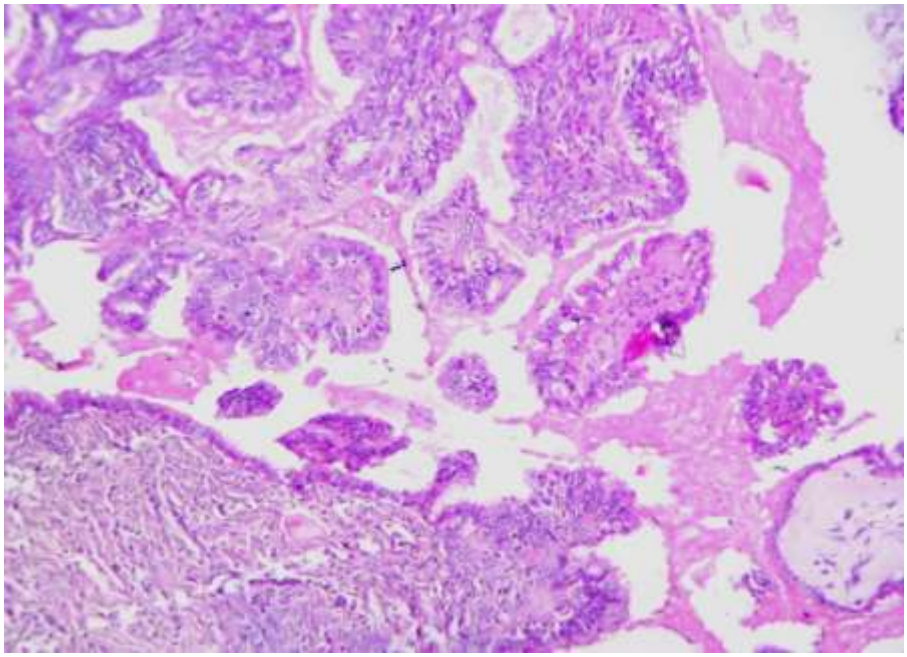


FIGURE 7: SEROUS BORDERLINE TUMOR WITH PAILLARY FRONDS LINED BY CELLS WITH MILD TO MODERATE ATYPIA WITHOUT STROMAL INVASION.( H&E-10X).

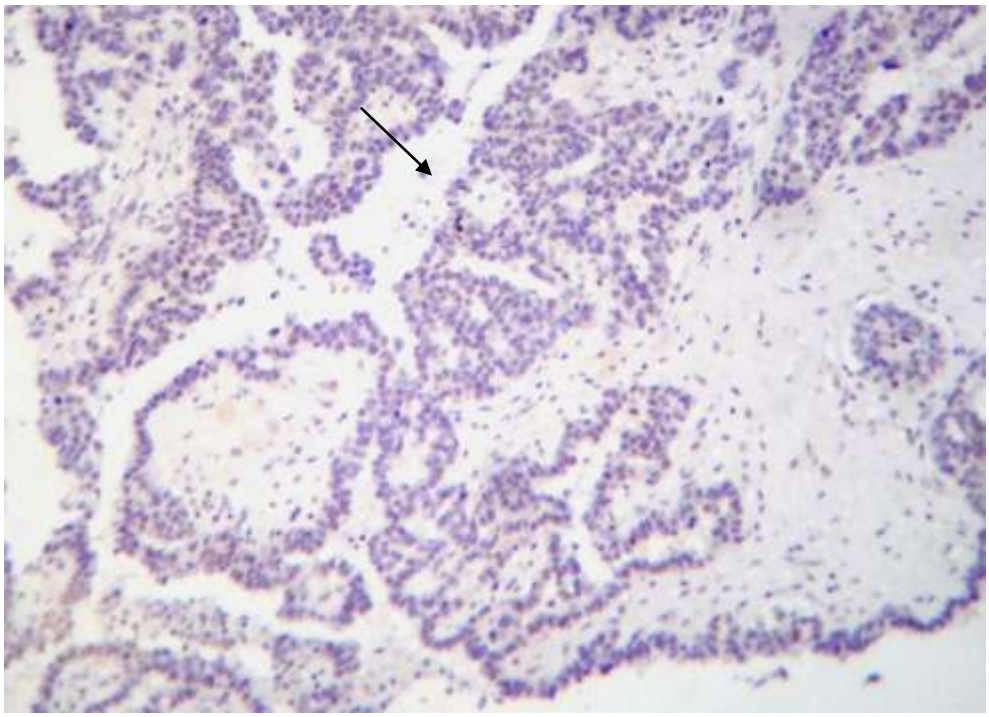


FIGURE 8: LOW GRADE SEROUS CARCINOMA SHOWING BROAD PAPPILLARY FRONDS LINED BY CELLS WITH MILD TO MODERATE ATYPIA (H&E-10X).

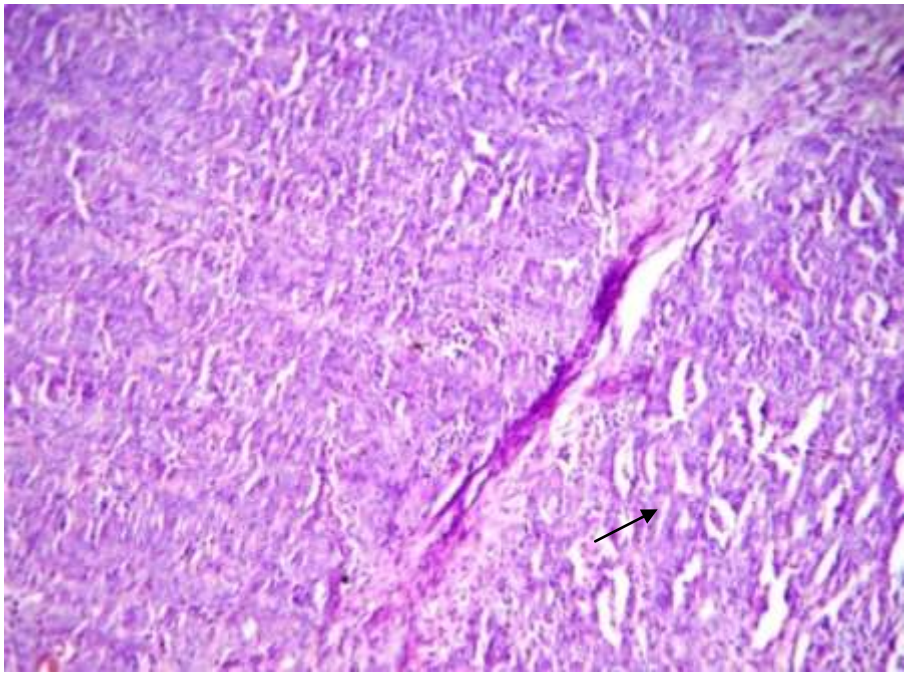


FIGURE 9A: HIGH GRADE SEROUS CARCINOMA WITH SOLID PROLIFERATION OF TUMOR CELLS AND FOCAL GLANDULAR ARCHITECTURE (ARROW) (H&E- 10X)

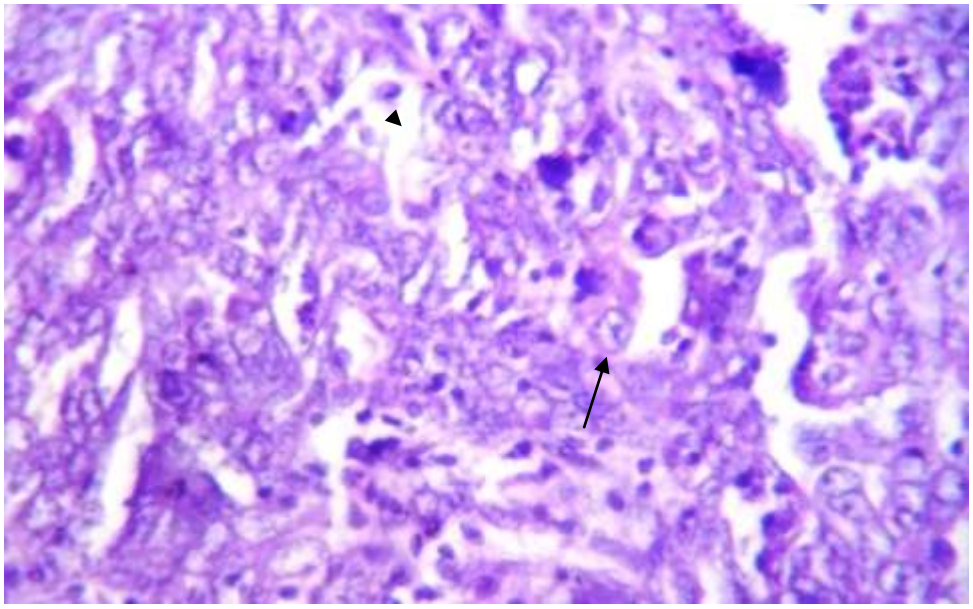


FIGURE 9B: HIGH GRADE SEROUS CARCINOMA- CLOSELY PACKED PAPILLAE WITHOUT FIBROUS CORE AND CELLS SHOW MARKED NUCLEAR ATYPIA AND PROMINENT NUCLEOLI WITH INCRASED MITOSIS (H&E - 45X).

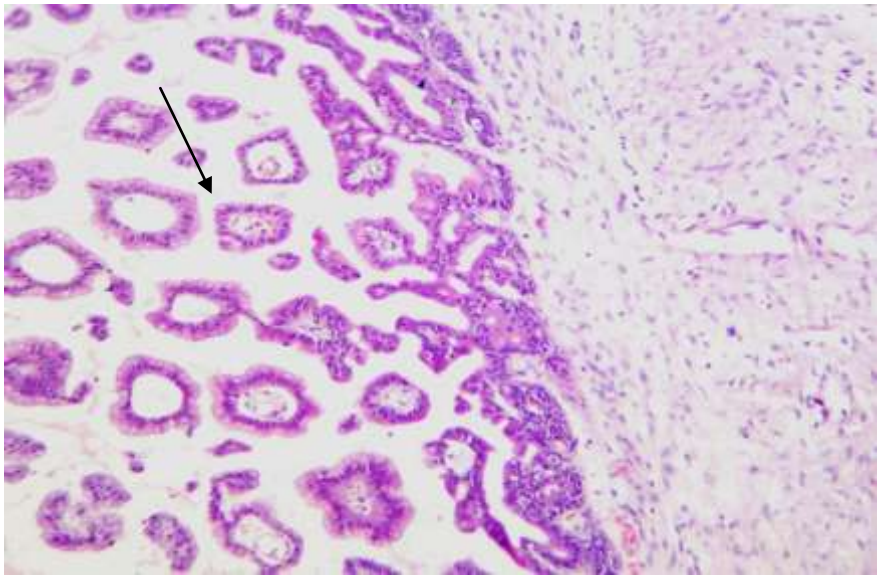


FIGURE 10A : MUCINOUS BORDERLINE TUMOR- SHOWING PAPILLARY FRONDS LINED BY MUCIN CONTAINING COLUMNAR EPITHELIUM WITH GOBLET CELLS- INTESTINAL TYPE (H&E- 10X)

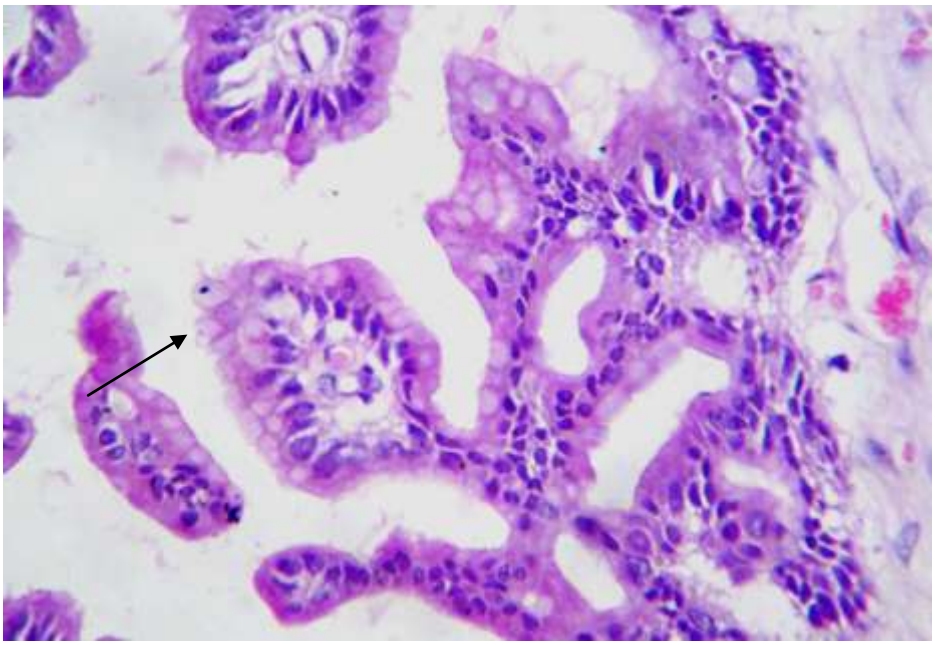


FIGURE 10 B : MUCINOUS BORDERLINE TUMOR –INTESTINAL TYPE.HIGH POWER VIEW SHOWING GOBLET CELLS (H&E- 45X)

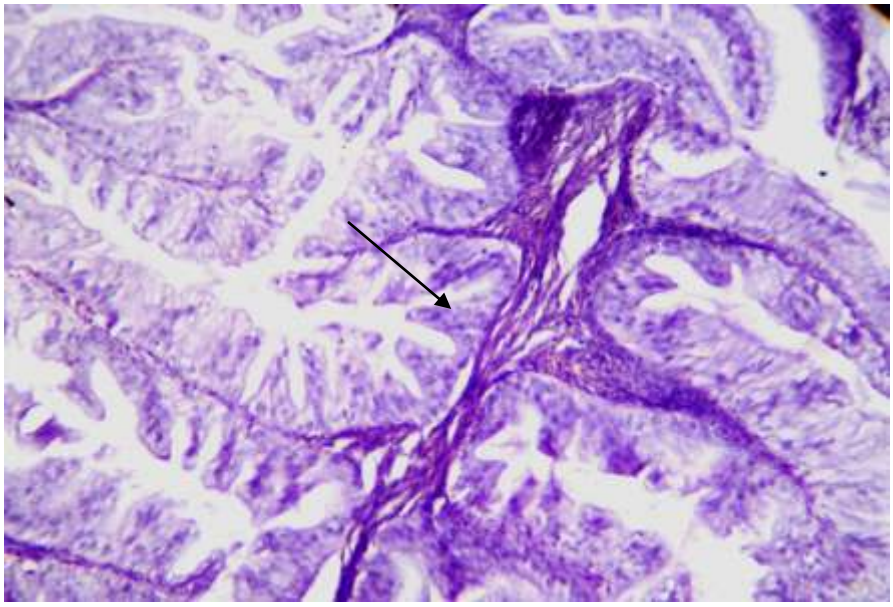


FIGURE 11 A: MUCINOUS CARCINOMA SHOWING EXPANSILE INVASION – CLOSELY PACKED(BACK-BACK) GLANDS WITH LITTLE/NO STROMAL SUPPORT (H&E- 10X)

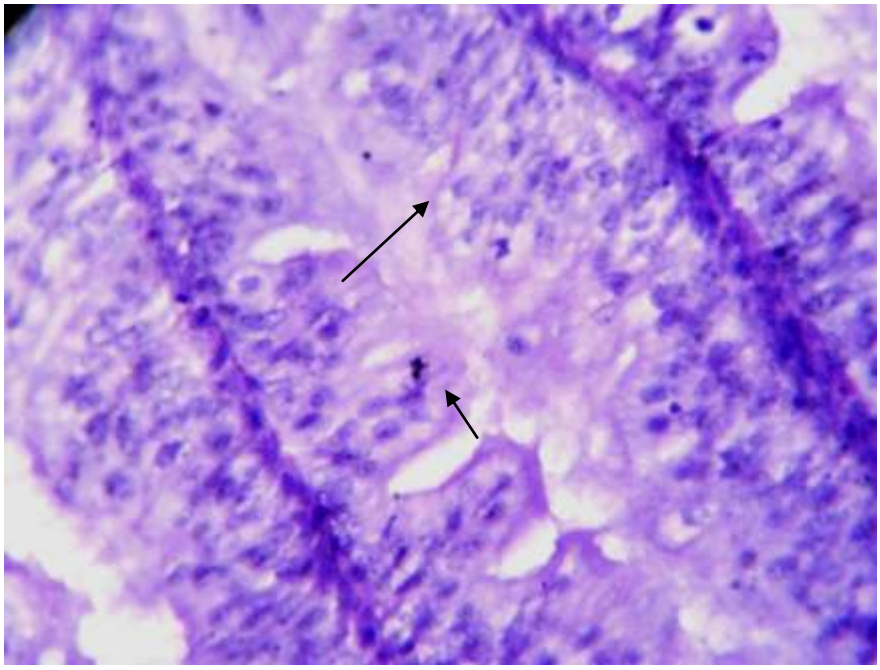


FIGURE 11 B : HIGH POWER VIEW : TUMOR CELLS SHOWING STRATIFICATION(>3LAYERS) OF NUCLEI WITH MITOTIC ACTIVITY (SMALL ARROW) (H&E- 45X).

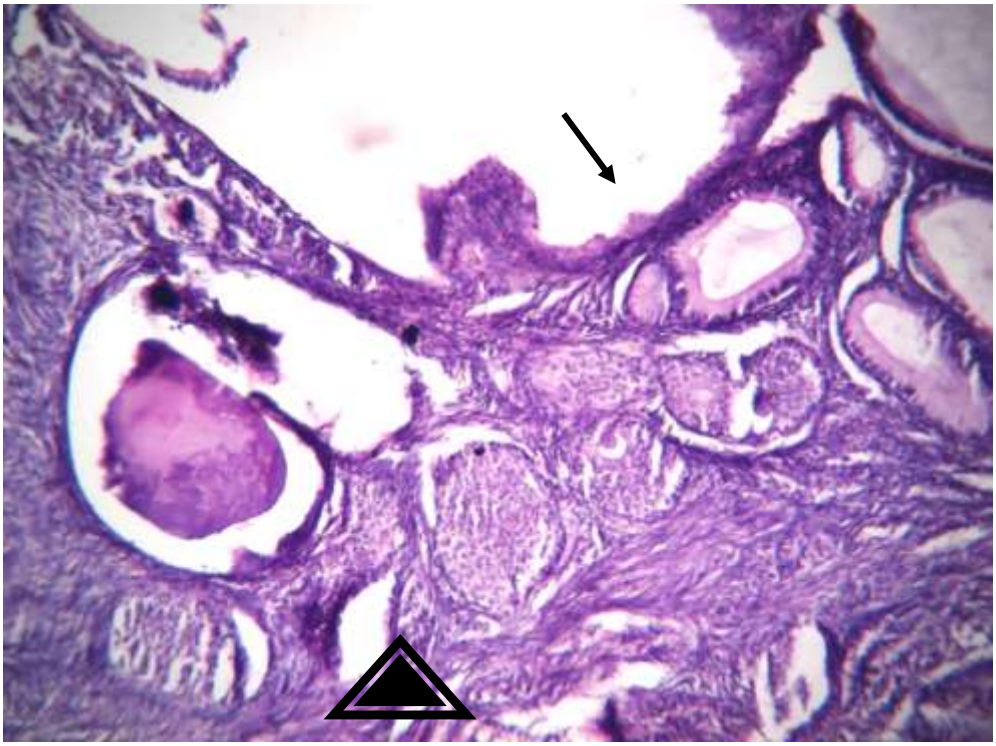


FIGURE 12 : MUCINOUS CYSTADENOMA WITH BENIGN BRENNER COMPONENT- SHOWING GLANDS LINED BY MUCIN CONTAINING COLUMNAR EPITHELIUM WITH NESTS(ARROW HEAD) OF TRANSITIONAL EPITHELIAL CELLS (H&E- 10x)

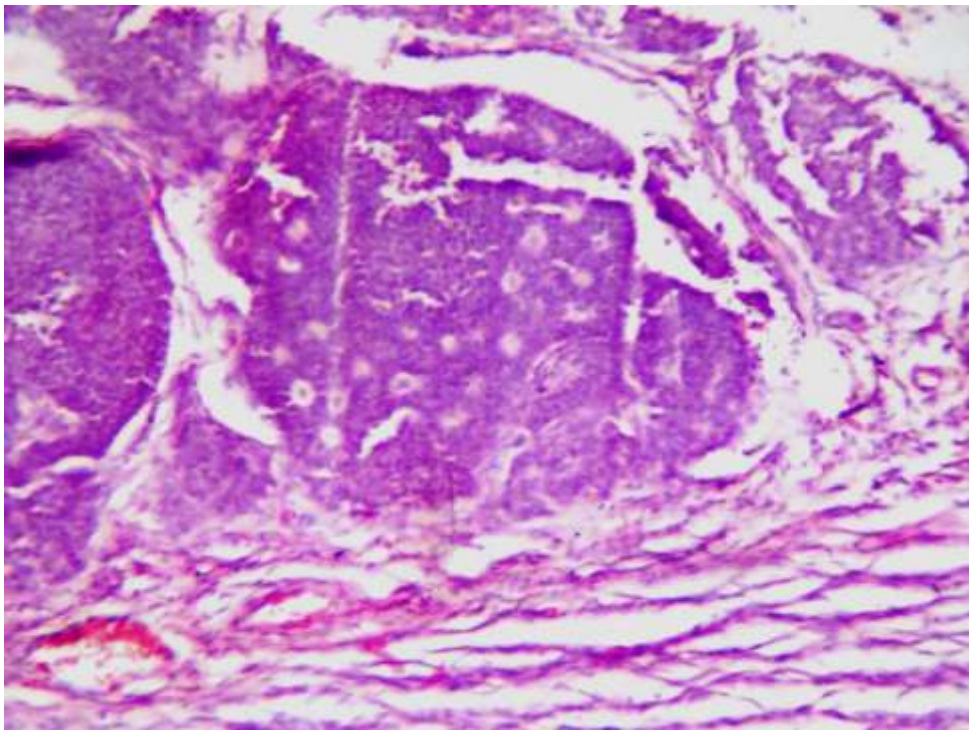


FIGURE 13 A: WELL DIFFERENTIATED GRANULOSA CELL TUMOR WITH, MICROFOLLICULAR PATTERN (H&E- 10X)

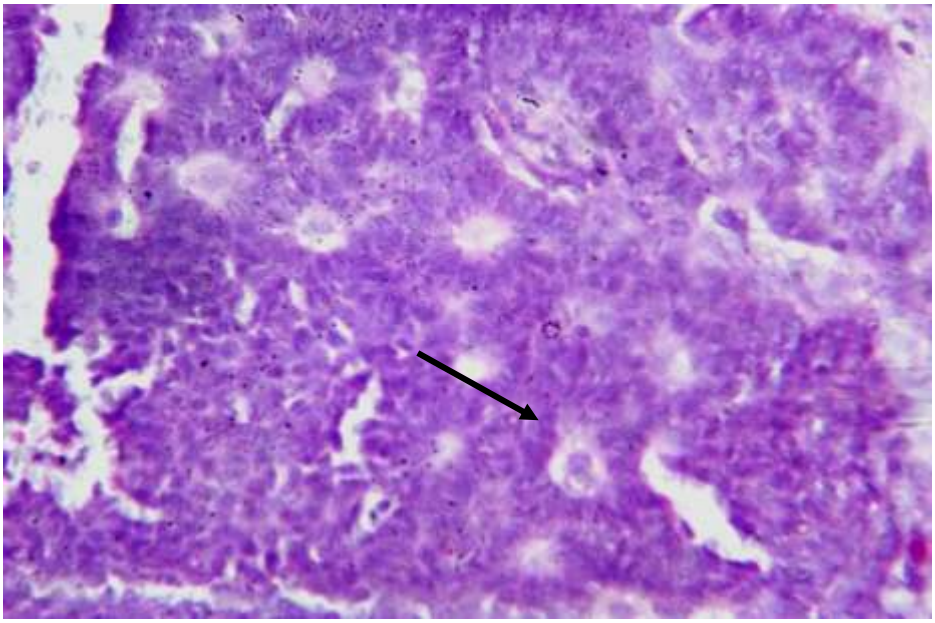


FIGURE 13 B: HIGH POWER VIEW SHOWING NUMEROUS CALL- EXNER BODIES CONTAINING HYALINE MATERIAL (H&E- 45X).

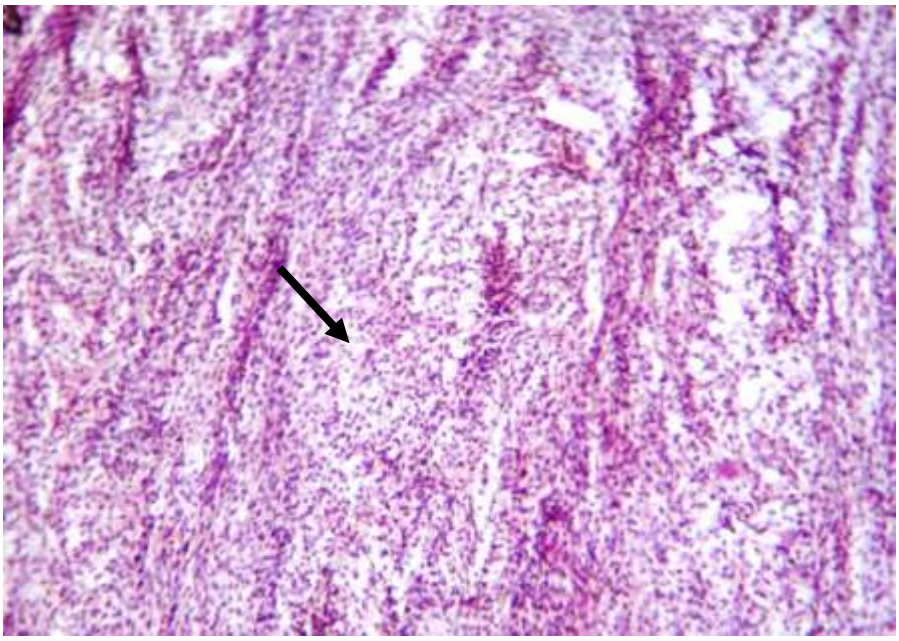


FIGURE 14: FIBROTHECOMA SHOWING FASCICLES OF SPINDLE CELLS ADMIXED WITH NUMEROUS LUTENISED CELLS (ARROW) WITH PALE VACUOLATED CYTOPLASM.(H&E-10X).

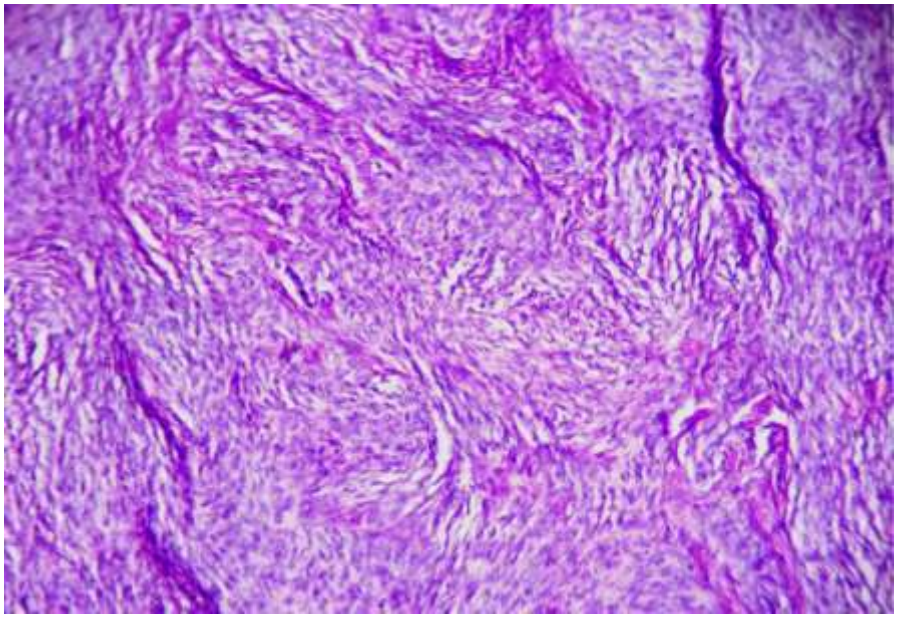


FIGURE 15: OVARIAN FIBROMA SHOWING, SPINDLE CELLS ARRANGED IN STORIFORM PATTERN WITH BLAND NUCLEAR FEATURES(10X).

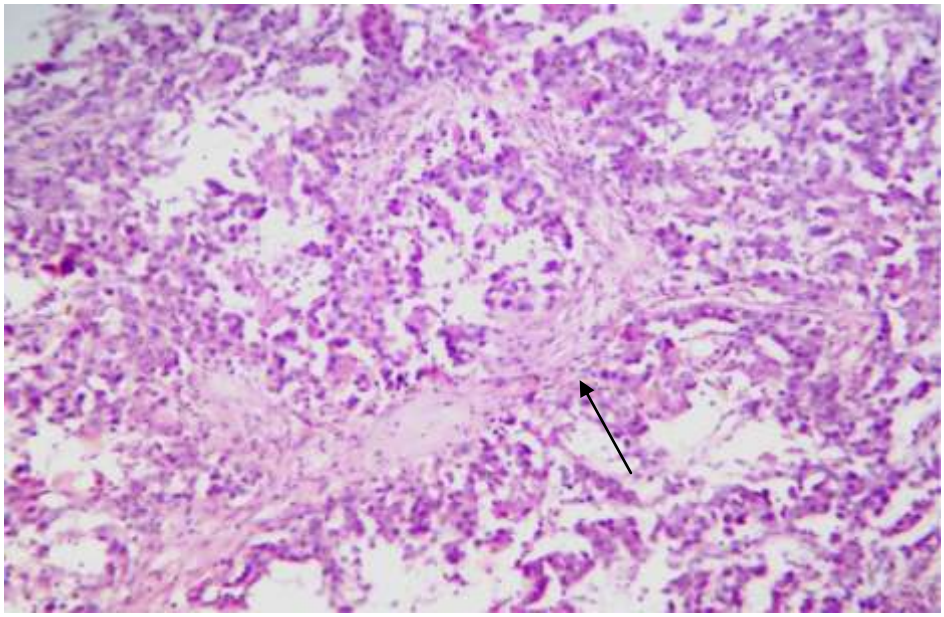


FIGURE 16: DYSGERMINOMA.IRREGULAR ISLANDS OF CELLS SEPARATED BY FIBROUS SEPTA(ARROW) INFILTRATED WITH LYMPHOCYTES. (H&E- 10X).

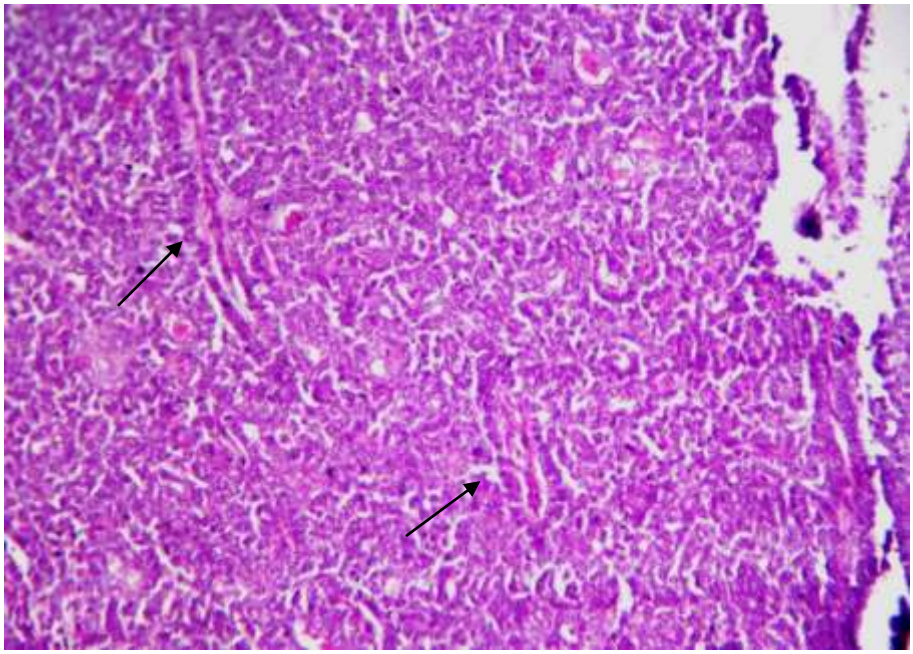


Figure17A :MIXED GERM CELL TUMOR, EXHIBITING YOLK SAC COMPONENT, FESTOON PATTERNENDODERMAL SINUS IS SEEN ( H&E- 10x).

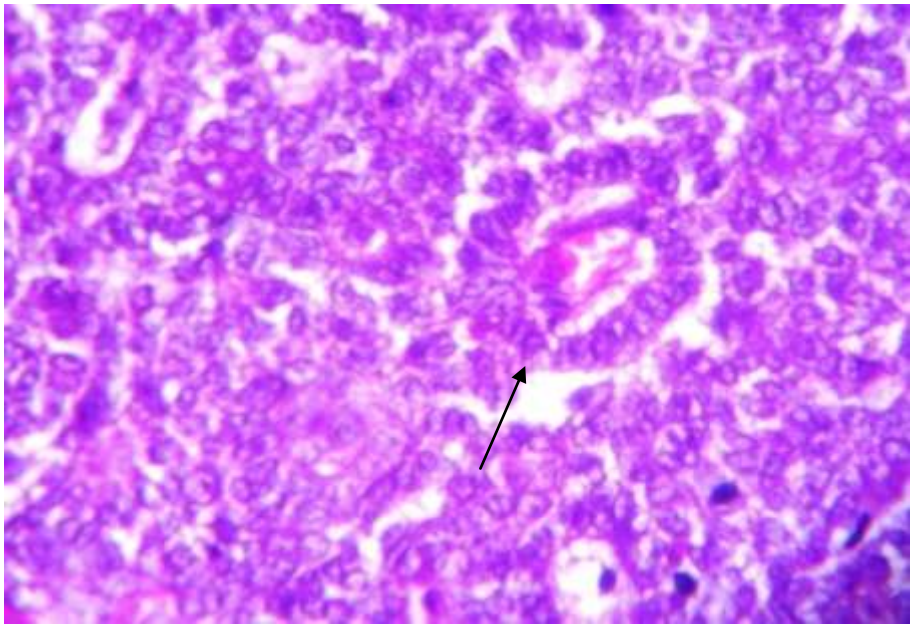


FIGURE 17 B: HIGH POWER VIEW SHOWING SCHILLER-DUVAL BODIES .(H&E- 45x).

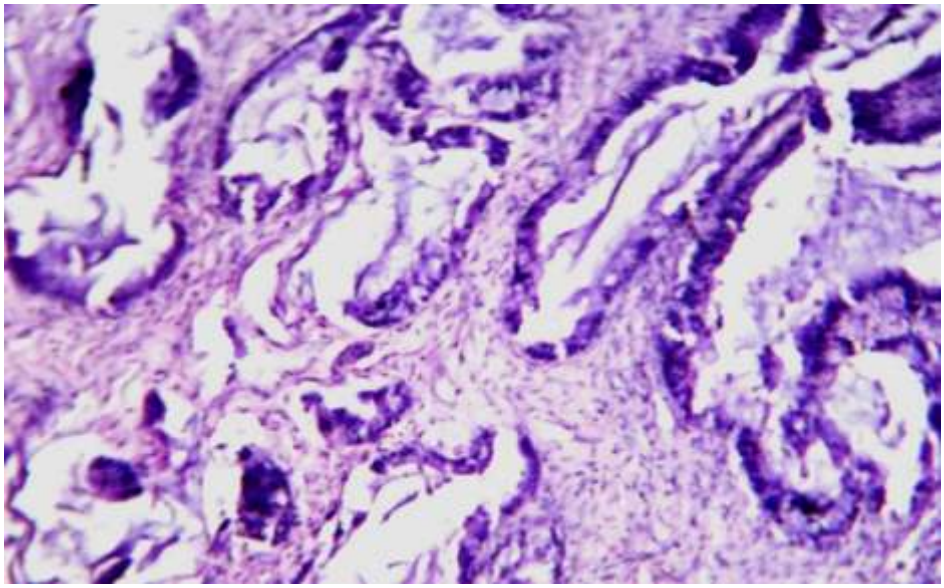


FIGURE 18: METASTATIC ADENOCARCINOMATOUS DEPOSITS . MALIGNANT GLANDS LINED BY ATYPICAL COLUMNAR EPITHELIUM WITH LUMINAL AND INTRACYTOPLASMIC MUCIN RESEMBLING GIT EPITHELIUM INFILTRATING INTO OVARIAN STROMA (H&E - 10X).

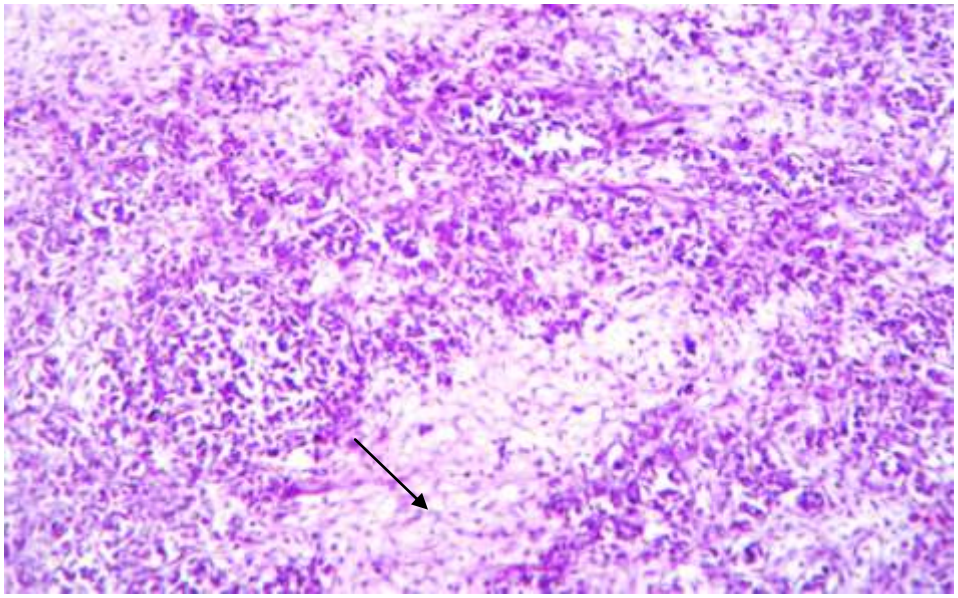


FIGURE 19: KRUKENBERG TUMOR - SHOWING SIGNET RING CELLS (H&E- 10X)

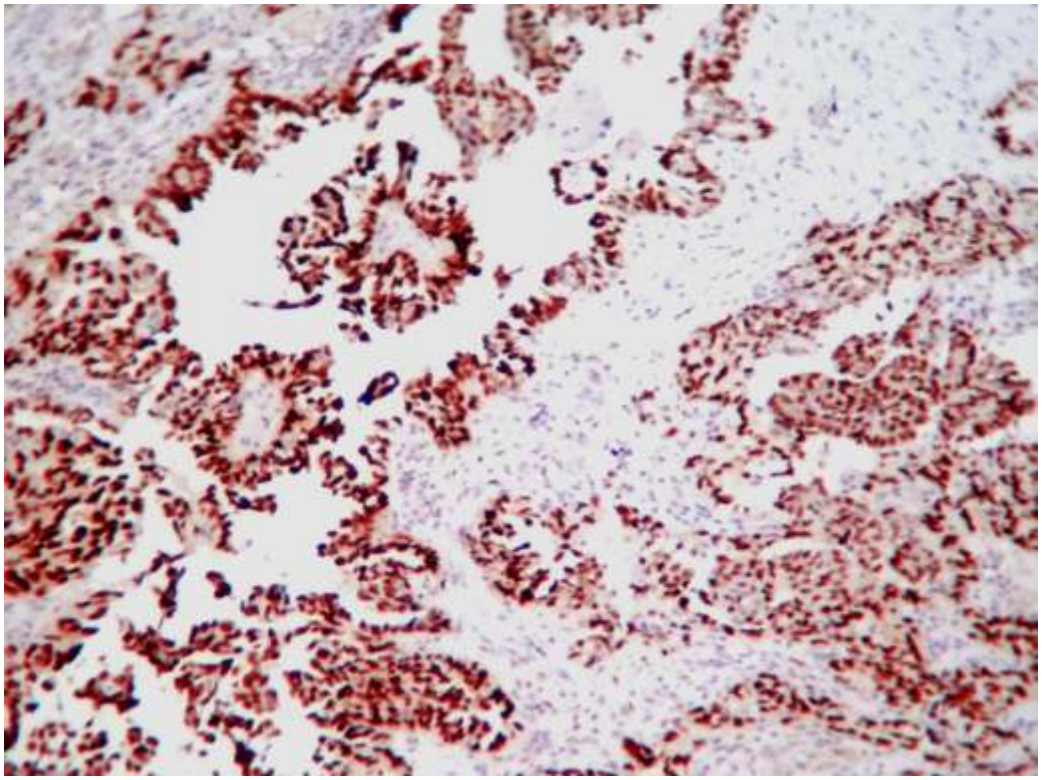


Figure 20: HIGH GRADE SEROUS CARCINOMA- DIFFUSE p53 NUCLEAR STAINING(10X).

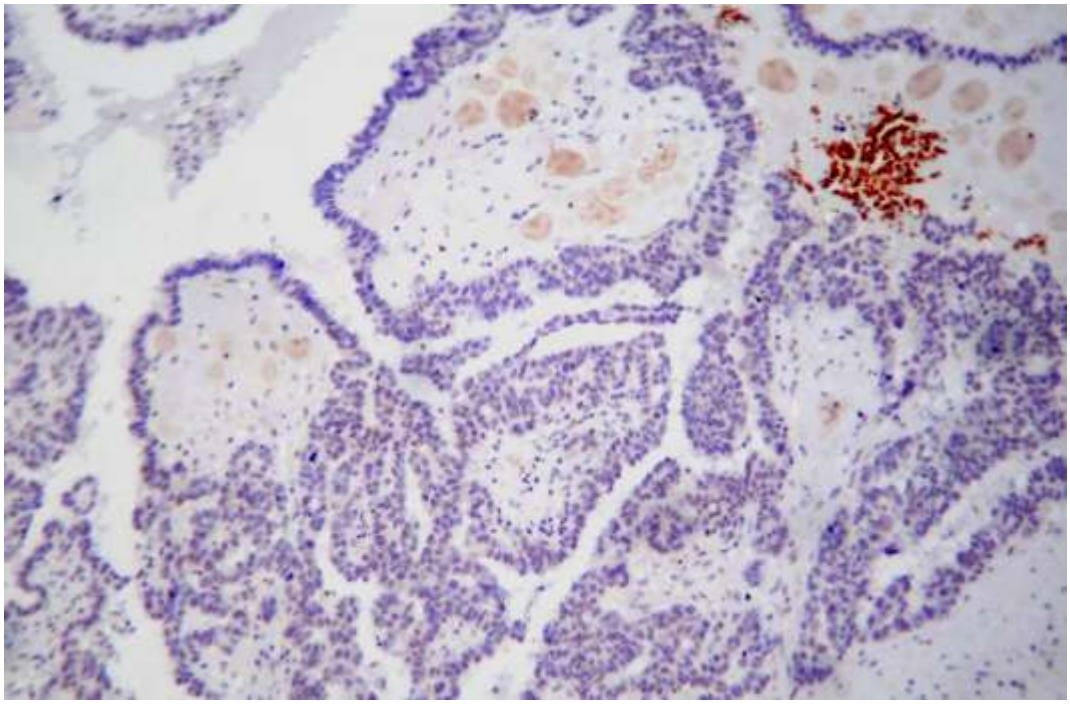


FIGURE 21: LOW GRADE SEROUS CARCINOMA – NEGATIVE STAINING FOR p53 (10X).

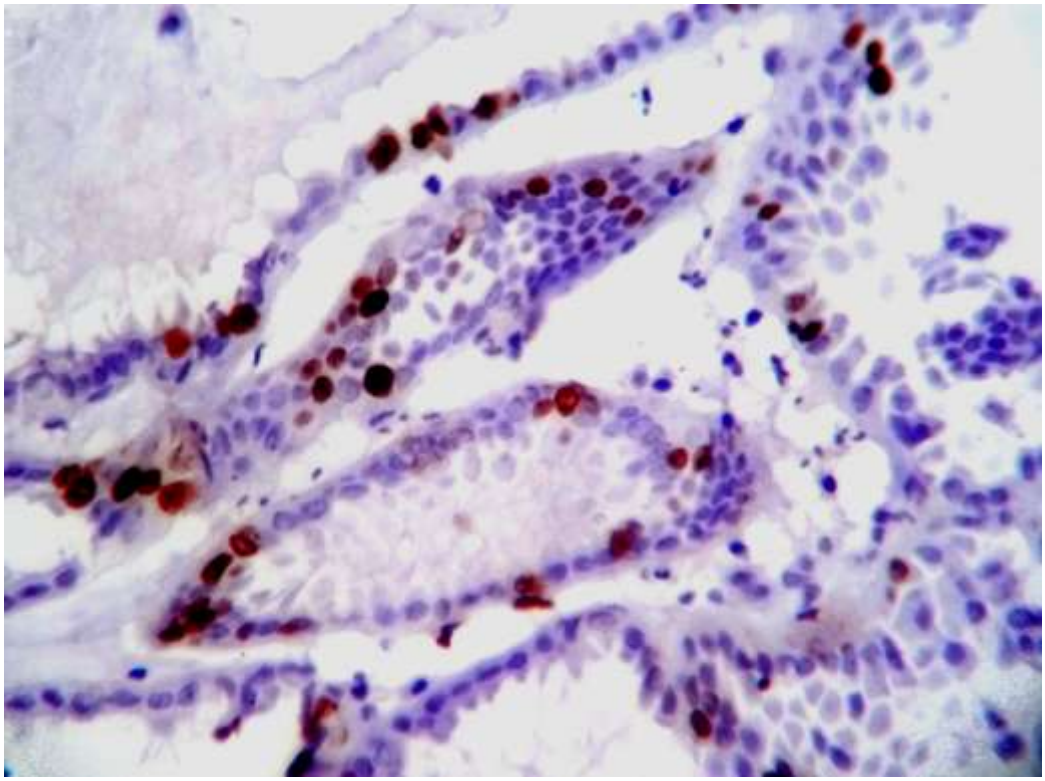


FIGURE 22: SEROUS BORDERLINE TUMOR –Ki 67 LI –19% (45X).

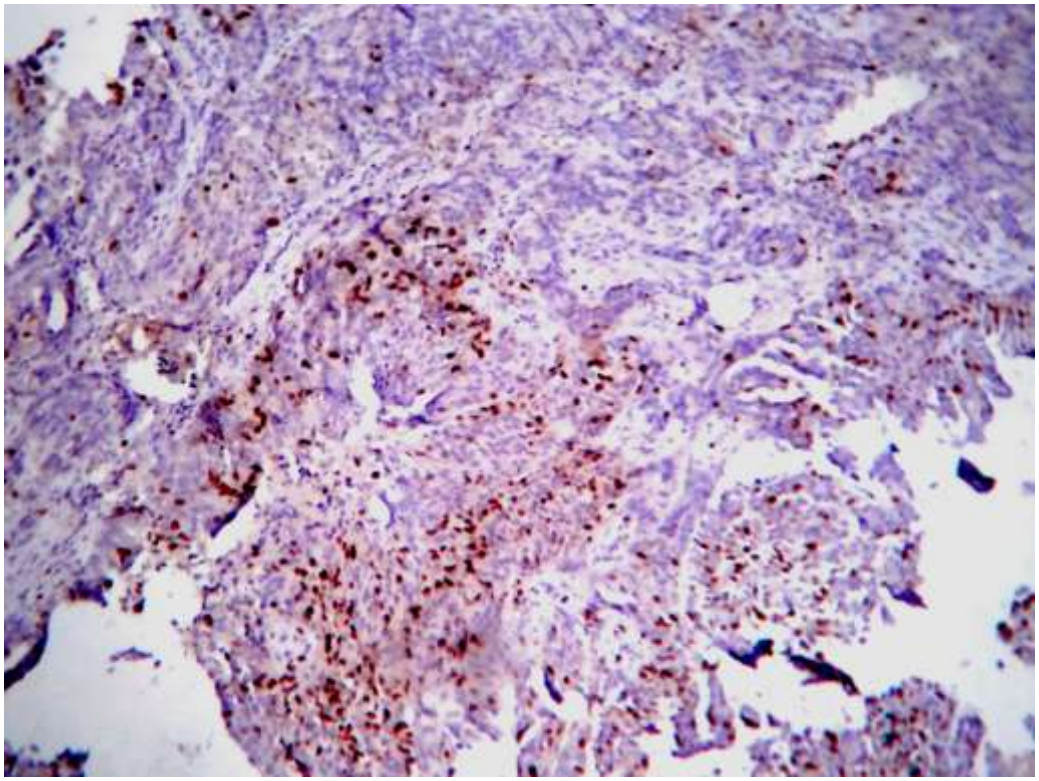


FIGURE 23: SEROUS CARCINOMA Ki-67 STAINING. LI- 42 % (10X).

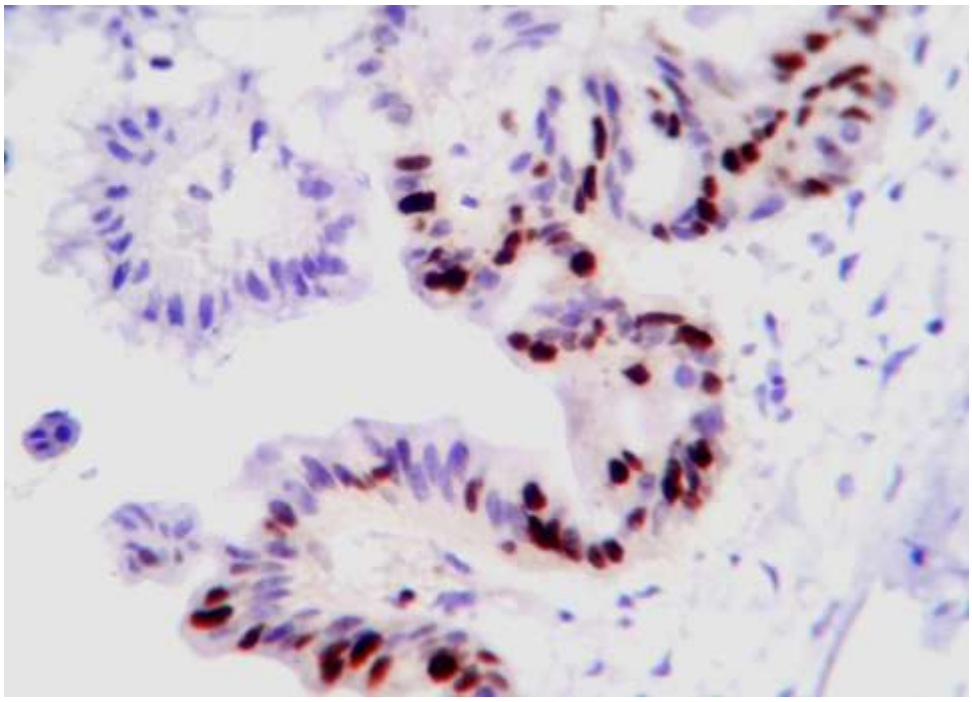


FIGURE 24 A: MUCINOUS BORDERLINE TUMOR  Ki-67 STAINING LI- 22%( 45X)

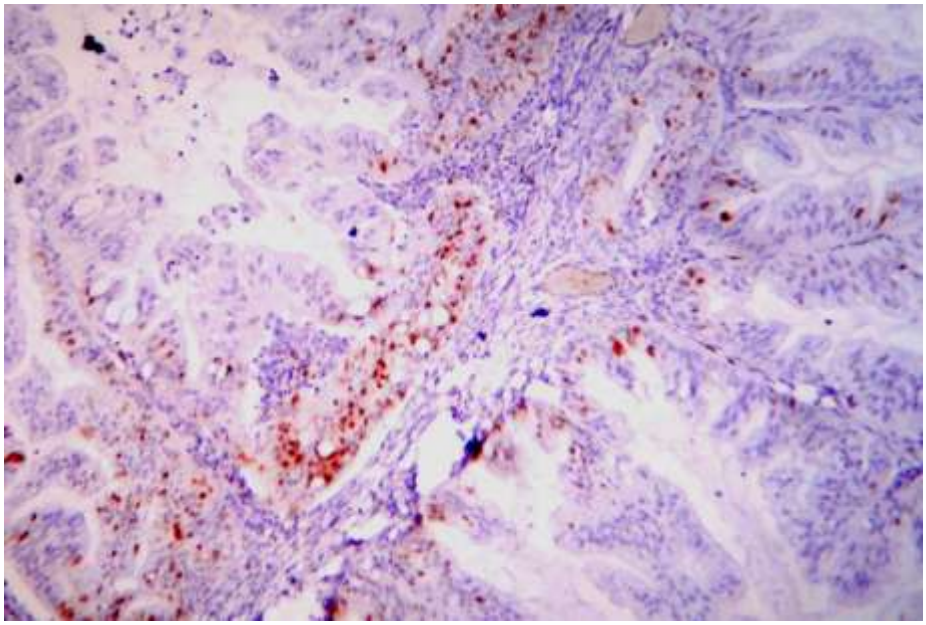


FIGURE 24 B: MUCIONUS BORDERLINE TUMOR Ki-67 STAINING  LI- 28%.(10X)

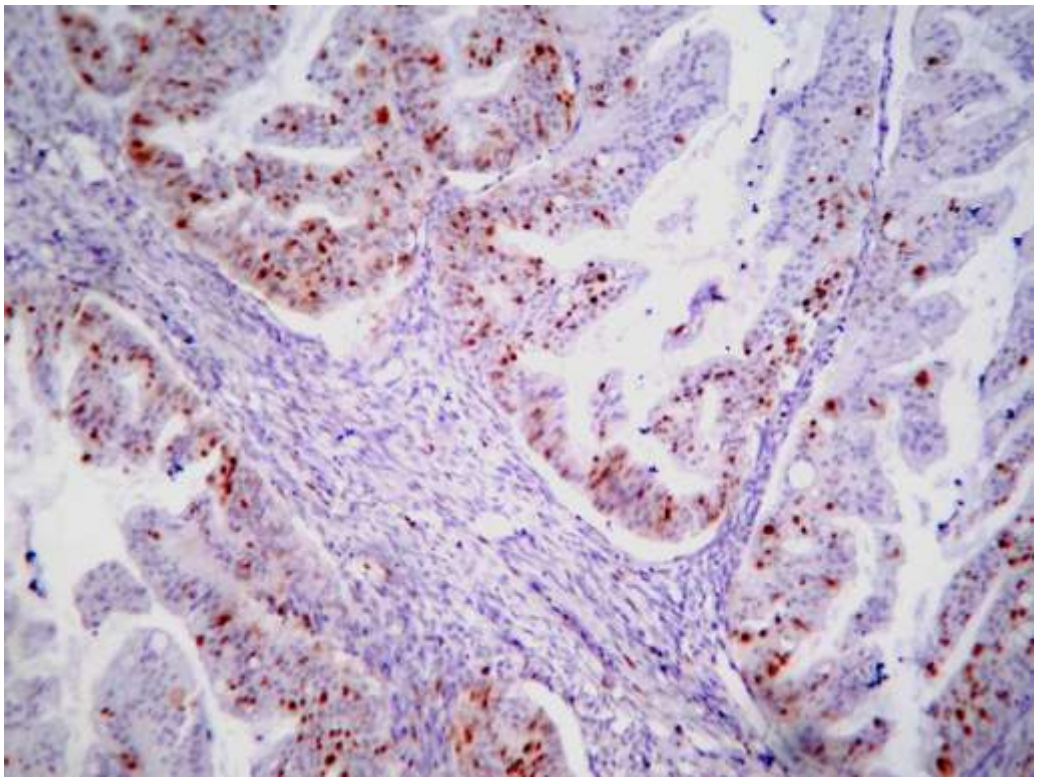


FIGURE 25: MUCINOUS CARCINOMA Ki-67 STAINING LI- 36%.(10X)

# DISCUSSION

# DISCUSSION

Ovaries are common sites of non-neoplastic and neoplastic lesions[83]. The anatomy of ovary is complex and its physiology peculiarly shows constant cyclical changes from puberty to menopause giving rise to different cell types, each of which is capable of giving rise to complex varieties of tumors[32].

Two thirds of ovarian tumors occur in women of reproductive age group[92]. According to Glen mc clugge et al ovarian cancer is considered to be a silent Killer, as most of these tumors are identified at advanced stage of the disease(FIGO III or IV)and hence overall prognosis is poor[32].

Although ovarian tumors are considered as one disease clinically; it is being increasingly realised that the different morphological subtypes has different pathogenesis and are associated with distinct molecular alterationsand have different prognosis[24].

In this study, about 11,726 surgical pathology specimens werereceived and analysed over a period of 2 1/2 years. Of these 626 weregynaecological tumors, among which ovarian neoplasms constitutes 150cases, accounting for about 23.9% of all gynaecological tumors.

## I.INCIDENCE:

In our study we observed that the ovarian malignancy accounted for **2.6%**of all female malignancies and is given in the following table.19 [CHART11]

**TABLE:19 : INCIDENCE OF MALIGNANT OVARIAN TUMORS IN RELATION TO TOTAL MALIGNANCIES IN FEMALES.**

| SL.NO | PERIOD | TOTAL NO OF MALIGNANCIES IN FEMLAES | TOTAL NO OF MALIGNANT OVARIAN NEOPLASMS | % |
|---|---|---|---|---|
| 1. | Jan10-May10 | 276 | 7 | 0.6% |
| 2. | Jun10-Dec10 | 242 | 6 | 0.5% |
| 3. | Jan11-May11 | 189 | 7 | 0.6% |
| 4. | Jun11-Dec11 | 277 | 5 | 0.4% |
| 5. | Jan12-May12 | 106 | 4 | 0.3% |
| | Total | 1090 | 29 | 2.6% |

**CHART 11: INCIDENCE OF MALIGNANT OVARIAN TUMORS IN RELATION TO TOTAL FEMALE MALIGNANCY**

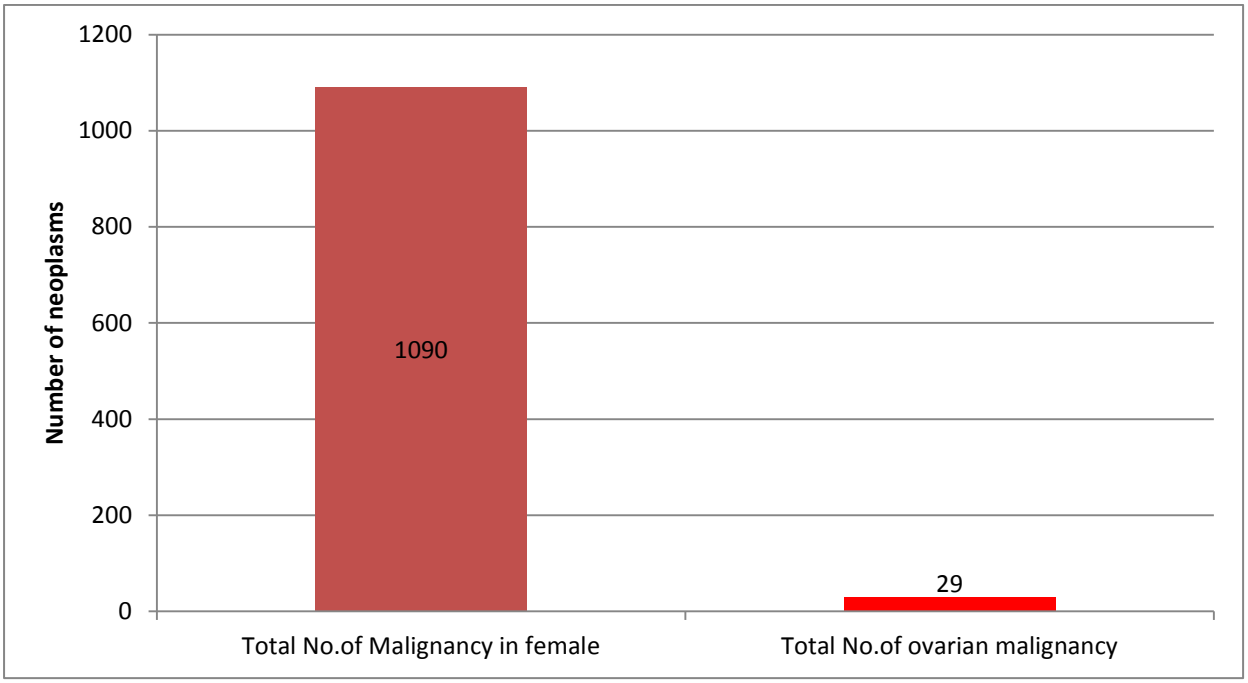
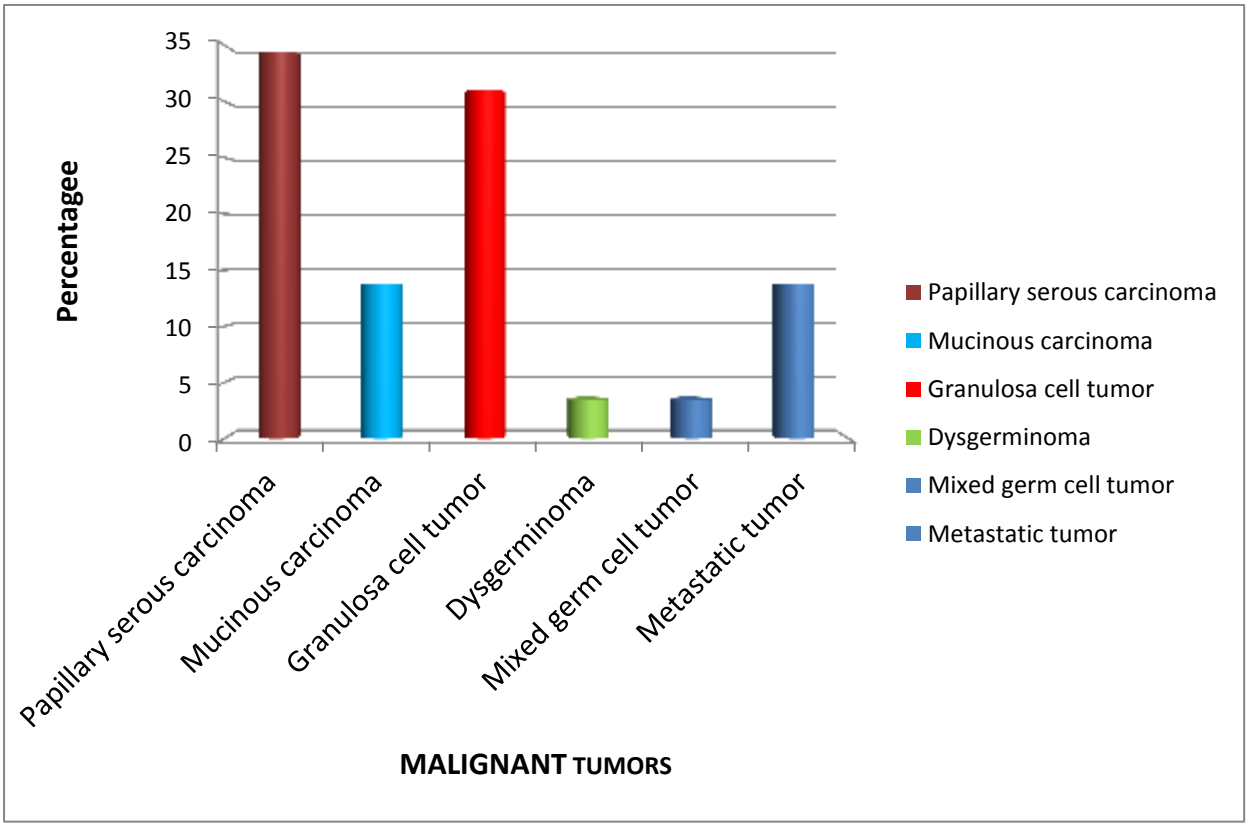


**CHART 12: INCIDENCE OF INDIVIDUAL MALIGNANT OVARIAN TUMORS**



**II : INCIDENCE OF HISTOLOGICAL TYPES OF MALIGNANT TUMORS IN RELATION TO TOTAL OVARIAN MALIGNANCIES.**

**TABLE 20:**

| HISTOLOGICAL TYPE | NO.OF CASES | % of Total Malignant Ovarian Tumors(29) | % Incidence of Total Ovarian tumors(150) |
|---|---|---|---|
| Papillary Serous cystadenocarcinoma | 10 | 34.4 | 6.6 |
| Mucinous cystadenocarcinoma | 4 | 13.7 | 2.6 |
| Granulosa Cell Tumor | 9 | 31.03 | 6 |
| Dysgerminoma | 1 | 3.44 | 0.6 |
| Mixed germ cell tumor | 1 | 3.44 | 0.6 |
| Metastatic adeno/krukenberg | 4 | 13.7 | 2.6 |

From the above table.20 it is evident that , of the total 29 malignant ovarian tumors , most common was papillary serous cystadenocarcinoma accounting for about 34.5%(10/29) , followed by granulosa cell tumor accounting for 31 %(9/29) and mucinous adenocarcinoma & metastatic tumors

accounting for 13%(4/29) each. The least common type in this study was dysgerminoma(1/29 cases). [CHART 12].

## III. INCIDENCE OF OVARIAN CARCINOMA IN RELATION TO OTHER STUDIES

**TABLE 21:**

| SL.NO | PLACE OF STUDY | INCIDENCE |
|---|---|---|
| 1. | Grant medical college and sir J.J group of hospitals ,Mumbai | 7.8% |
| 2. | Dr.BR Ambedkar institute hospital, New delhi | 7.5% |
| 3. | Adyar cancer institute,Chennai | 5.1% |
| 4. | Chittaranjan National cancer institute | 5.8% |
| 5. | Dindigul ambilikai cancer registry | 3.3% |
| 6. | Barshi rural registry,Maharashtra | 3.8% |
| 7. | Present study | 2.6% |

It is evident from the above table. 21 .that Mumbai holds the top ranking with the incidence rate of 7.8% and the least is Dindigul ambilikai cancer registry with the incidence rate of 3.3%. This study conducted in a semi urban area; showed an incidence rate of ovarian malignancy (2.6%) is in midway between rural and urban area. [CHART13].

## IV. INCIDENCE OF OVARIAN MALIGNANCIES IN RELATION TO FEMALE GENITAL TRACT MALIGNANCIES, TABLE 22:

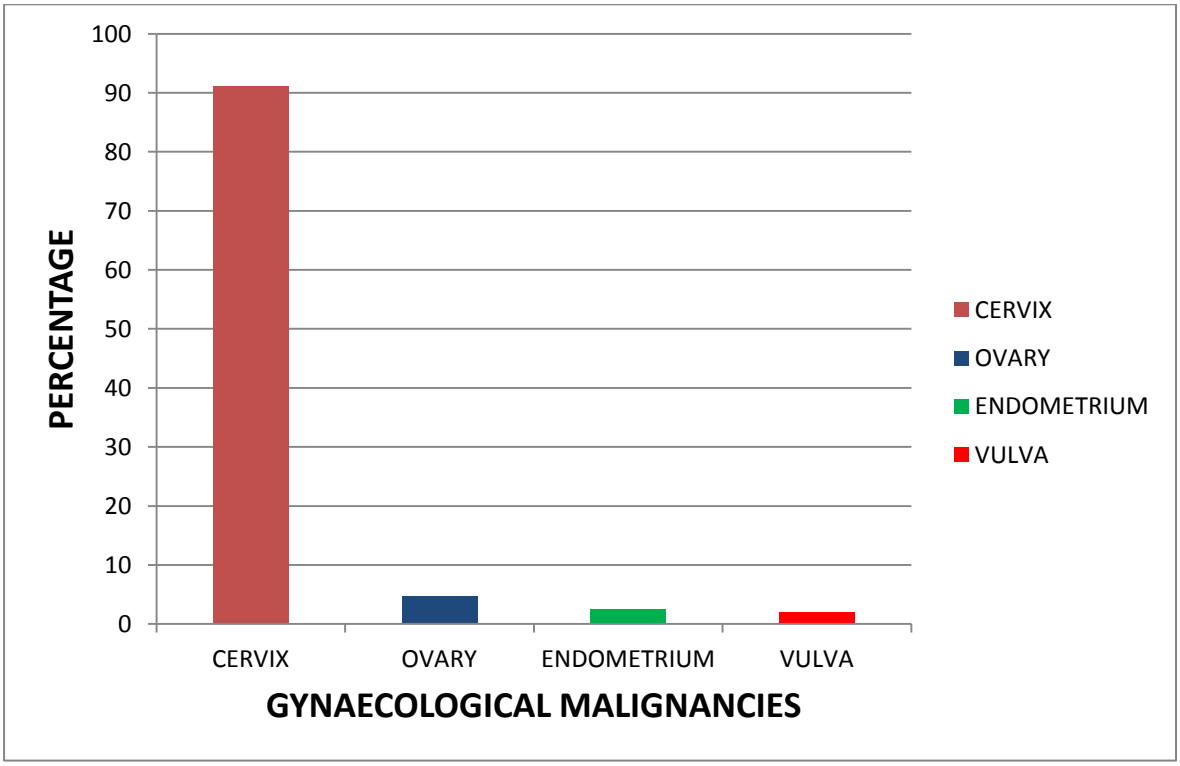
| SL.NO | SITE | NO.OF FEMALE GENITAL TRACT MALIGNANCIES | % |
|---|---|---|---|
| 1. | Cervix | 575 | 91% |
| 2. | Ovary | 29 | 4.7% |
| 3. | Endometrium | 16 | 2.5% |
| 4. | Vulva | 6 | 1% |
| 5. | Vagina | - | - |
| 6. | Fallopian tube | - | - |
| | Total | 626 | |

From the above table.22, it was observed that ovarian malignancies are the second common(4.7%) malignancy among all female genital tract malignancies. It was also observed that uterine cervix (91%) was found to be the first most common site to be involved , and the least common site is vulva.[CHART 14]

The age specific incidence of ovarian neoplasms ranges from 20-70 years . According to Min jae kim et al the incidence of benign neoplasms peaks in 2$^{nd}$ -3$^{rd}$ decade of life[93,94]. In this study, benign neoplasms were commonly observed in 20-29 yrs of age which is well correlated with our study. According to Debra et al, the incidence of borderline ovarian tumors peaks in 4$^{th}$ decade.

In our study borderline ovarian tumors are common in 40-50yrs age group. This finding is well correlated with previous studies and literature {6,21}.

**CHART 14: INCIDENCE OF OVARIAN MALIGNANCIES IN RELATION TO FEMALE GENITAL TRACT MALIGNANCIES**




In this study malignant ovarian tumors are common in $5^{th}$-$6^{th}$ decade. This in accordance with study conducted byshruti shah et al[88], who showed that 42.5% patients with malignant tumors were in the age group of 51-60yrs. Similar findings were noted in other studies [24,32].

Ovarian cancers are considered as a silent killer, as they present at an advanced stage of the disease due to the non specific symptoms. Most common presenting symptom in our study was abdominal mass(80%),followed by pain abdomen(7%). This is similar to a study conducted byHiermath et al in Pondicherry which showed that abdominal mass ispresenting symptom accounting for 84% cases followed by abdominal pain (12%).

In this study; 14 cases ,constituting for about 9% of all ovarian tumors showed bilateral involvement at the time of presentation. Of which 5 cases (35%) were benign, 1 case(7%) were borderline, 8 cases(57%) were malignant.

Among malignant tumors, bilaterality is commonly observed in malignant serous group (4/8, 50%), followed by metastatic tumor(3/8,37%). This is inaccordance with study conducted by R Jha et al[78]

· In this study, 72.6% ovarian tumors were benign and 19.3% were malignant. This is similar to the data from a study by Pilli et al in India which showed that 75.2% were benign, and a similar study conducted by samina et alin Pakistan which showed similar results with 78% benign tumors and 21 % were malignant. Comparison of incidence of benign and malignant ovarian tumors in our study in relation to various other studies are given in the following table 23.[ CHART15]

**CHART 15: INCIDENCE OF OVARIAN TUMORS IN RELATION TO OTHER STUDIES**

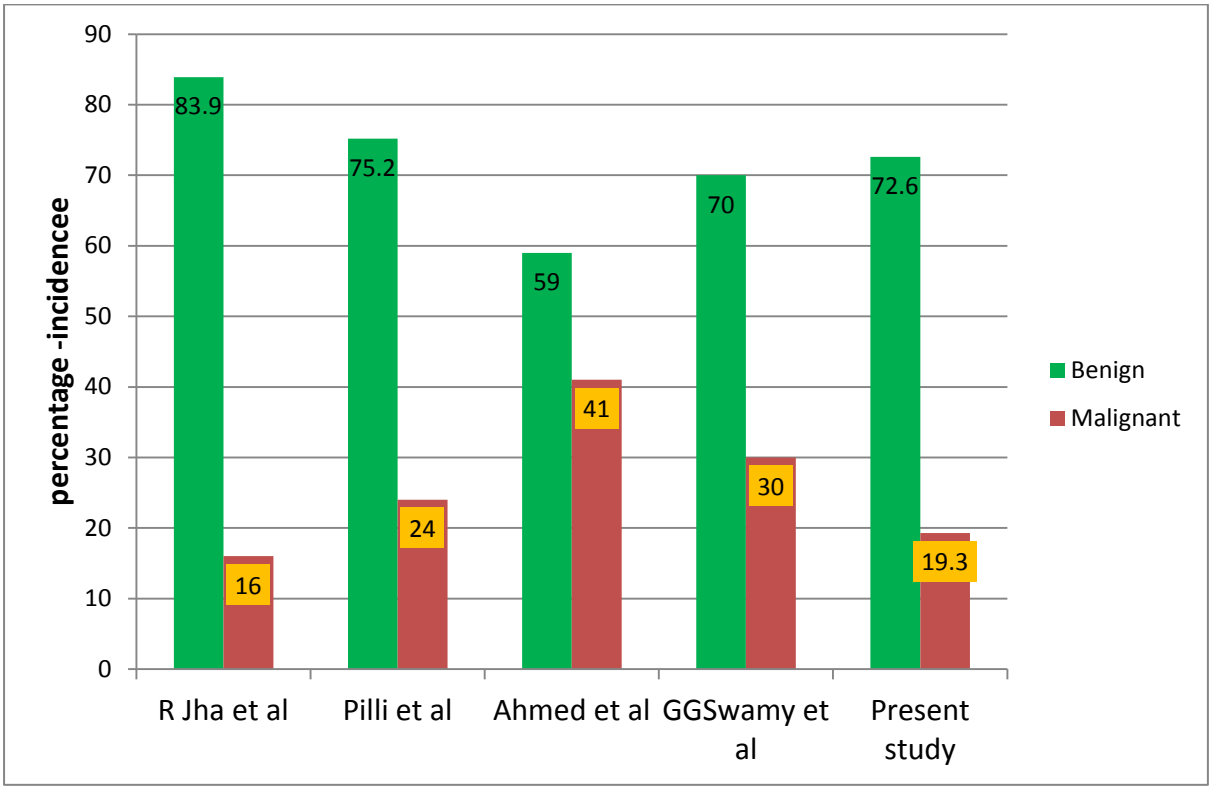
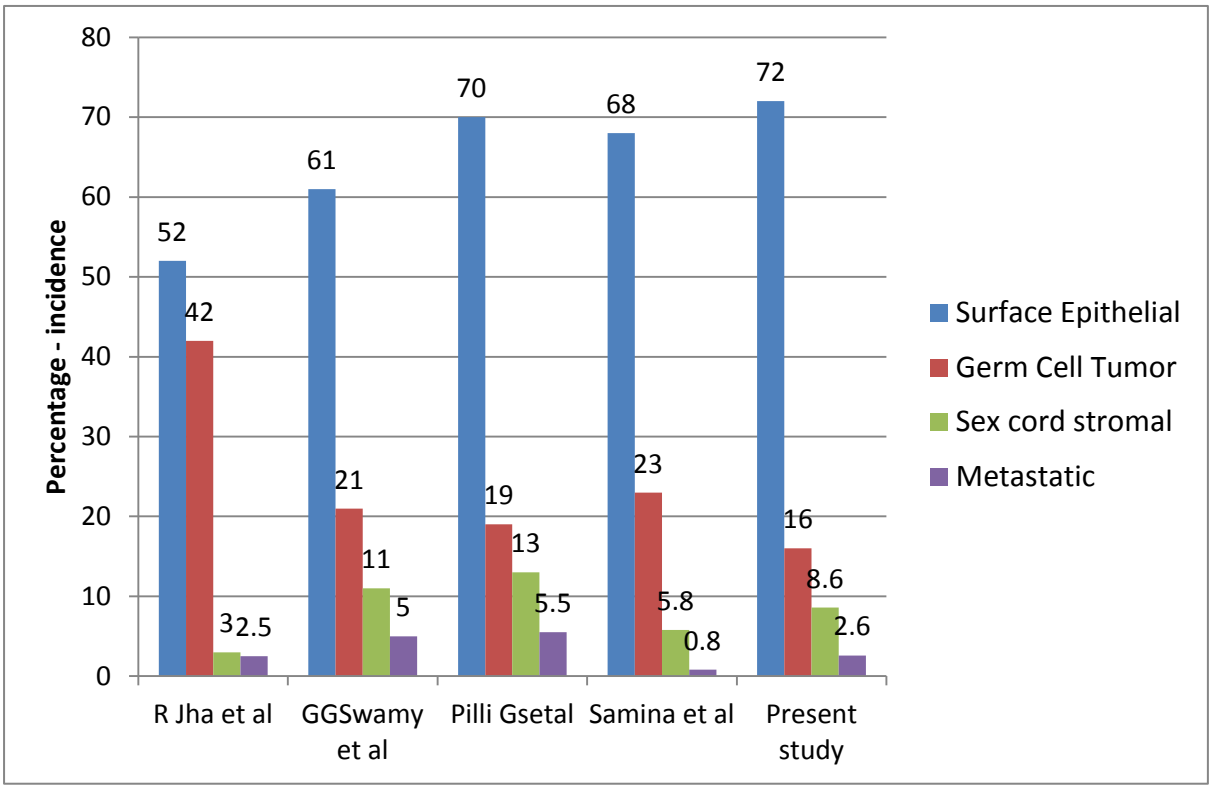


**CHART 16: COMPARING THE INCIDENCE OF HISTOLOGICAL TYPES OF OVARIAN TUMORS IN RELATION TO OTHER STUDIES**




## TABLE 23 : INCIDENCE OF OVARIAN TUMORS IN OUR STUDY IN RELATION TO OTHER STUDIES:

| Author | PLACE OF STUDY | BENIGN | MALIGNANT |
|---|---|---|---|
| R Jha et al | Nepal | 83.9% | 16% |
| Pilli et al | India | 75.2% | 24.8% |
| Ahmed et al | Pakistan | 59.2 % | 40.8% |
| GG Swamy et al | Nepal | 71.6% | 30% |
| Present study | Thanjavur | 72.6% | 19.3% |

Among all ovarian tumors ,surface epithelial tumors was the most common, accounting for about 72.6% followed by germ cell tumors(16%) and sex cord stromal tumors (8.6%).The data obtained in this study well correlates with the study conducted by sumaira et al in Pakistan which showed that surface epithelial tumors predominates with 76.5% ,followed by germ cell tumors(18%). Following table 24 compares the incidence of histological types of ovarian tumors in this study in relation to other study .[CHART16]

**TABLE 24 : COMPARISON OF INCIDENCE OF HISTOLOGICAL TYPES OF OVARIAN TUMORS WITH OTHER STUDIES.**

| Author | Place of study | Surface epithelial tumor | Germ cell tumor | Sex cord stromal tumor | Metastases |
|---|---|---|---|---|---|
| Samina et al | Pakistan | 68.5% | 23% | 8.6% | 2.6% |
| GG Swamy et al | Nepal | 61.6% | 21.7% | 11.7% | 5% |
| Pilli GS et al | India | 71% | 18% | 9.6% | 1.2% |
| Present study | Thanjavur | 72.6% | 16% | 8.6% | 2.6% |

In this study among the surface epithelial tumors , most common wereserous tumors accounting for 56% , followed by mucinous tumors (41%). Among serous tumors, 78.6% were benign, 4.9% were borderline,16.3% were malignant. This is in accordance with study conducted by R Jha et al inNepal which showed that benign serous tumors were the commonest (78.9%) followed by malignant serous tumors (22%). Following table.25 and 26 compares the incidence of histological subtypes of surface epithelial tumors in relation to other studies. [CHART17]

**CHART 17: COMPARING THE INCIDENCE OF HISTOLOGICAL SUBTYPES OF SURFACE EPITHELIAL TUMORS IN REALTION TO OTHER STUDIES**

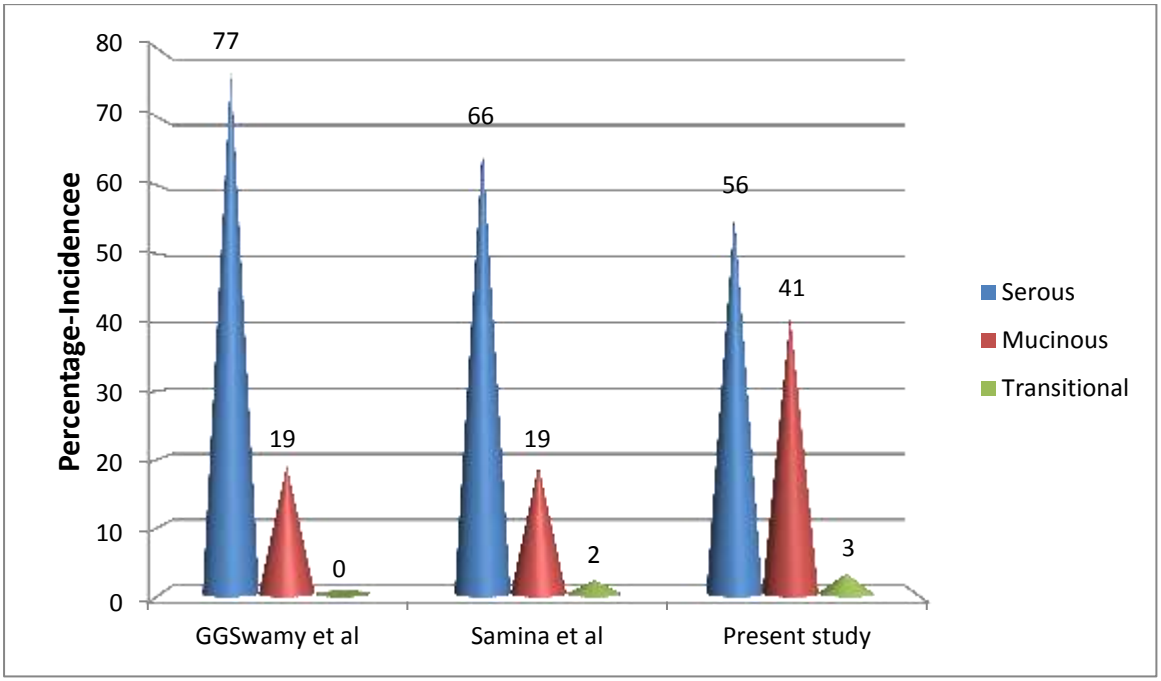


**CHART 18: COMPARING THE INCIDENCE OF SEROUS TUMORS IN RELATION TO OTHERSTUDIES**

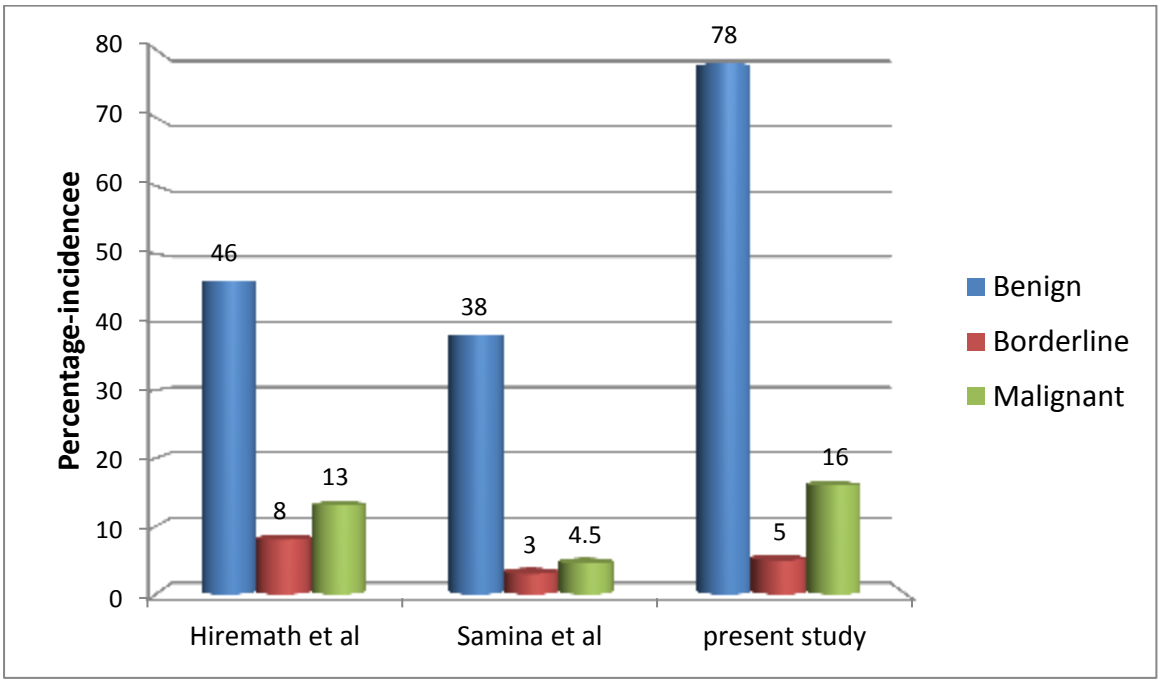



**TABLE 25: COMPARISON OF INCIDENCE OF HISTOLOGICAL SUBTYPES OF SURFACE EPITHELIAL TUMORS IN RELATION TO OTHER STUDIES:**

| AUTHOR | PLACE OF STUDY | SEROUS | MUCINOUS | TRANSITIONAL |
|---|---|---|---|---|
| GGSwamy et al | India | 77% | 19% | - |
| Samina et al | Pakistan | 66% | 18.7% | 2.2% |
| Present study | Thanjavur | 56% | 41.2% | 2.75% |

**TABLE 26 : COMPARISON OF INCIDENCE OF SEROUS TUMORS IN RELATION TO OTHER STUDIES.**

| AUTHOR | PLACE OF STUDY | BENIGN | BORDERLINE | MALIGNANT |
|---|---|---|---|---|
| Hiremath et al | Pondicherry | 46% | 8% | 13.5% |
| Samina et al | Pakistan | 38% | 2% | 4.5% |
| Fattaneh et al | India | 60% | 10% | 30% |
| Present study | Thanjavur | 78% | 5% | 16.3% |

According to the Jefferey et al[43] and Geza et al[21], Serous borderline ovarian tumors are the most common histological subtype of borderline tumors accounting for 65% of all borderline ovarian tumors[21]. In contrast, mucinous borderline tumors were common in our study accounting for about 75% cases and serous borderline for 25%.

According to Neeraj lalwani et al[65], approximately 1/3$^{rd}$ of serous borderline tumors are bilateral . In this study also 1/3$^{rd}$( 1case,33%) were bilateral. About 20-30% of serous borderline ovarian tumors were associated with peritoneal implants[21]. In contrast, in this study none of the serous borderline tumors had associated peritoneal implants at the time of presentation.

According to Glen mc cugage et al [24]& other studies, it is well established that there are two distinct types of serous carcinoma, namely low grade and high grade, low grade being much less common and arising from a serous borderline

tumor .In this study there are about 10 cases of serous carcinoma, of which 6 cases(60%) were high grade and 4 cases(40%) were of low grade was observed.

According to Anais malpaica et al[3],Ovarian serous carcinomas are classified into low grade and high grade according to recent 2-tier grading system, which is based primarily on the assessment of nuclear atypia with mitotic rate as a secondary feature. Recent 2 tier grading system is based on the evidence that low and high grade tumors arise from different genetic pathways[3].

According to Jefferay SD et al[44] surface epithelial tumors are classified into TypeI and Type II tumors which corresponds to two main pathways of tumorigenesis.

According to Russel vang et al[80] Type I tumors are indolent neoplasms that develop in a slow stepwise process from borderline tumors. They typically present as stage I tumors and remain as low grade tumors but can progress to high grade tumors. They include low grade serous carcinoma, mucinous carcinoma, endometroid carcinoma, malignant Brenner tumor and clear cell carcinomas[80].

In contrast type II tumors are high grade, arise as denovo, rapidly evolving , aggressive neoplasms and they typically present as advanced stage

disease[76,80]. They include high grade serous carcinoma, Malignant mixed mullerian tumor and undifferentiated carcinoma.

In addition to clinical and pathological differences between low grade and high grade serous carcinoma, they are also characterised by distinctive molecular genetic changes[80]. Low grade serous carcinomas typicallyshows KRAS & BRAF mutations and lack p53 mutations[73]. High grade seroustumors are characterised by p53 mutations and lack KRAS & BRAF mutations[73].

In this study mucinous tumors are the second most common type of surface epithelial tumors, of which 70% are benign,21% are borderline and 9% are malignant. This is in contrast to journals and literature where borderline mucinous tumors accounts for only 10% and malignant mucinous tumors also accounts for 10 % of tumors[76]. Following table .27compares the incidence of mucinous tumors in relation to other studies. [chart19].

**CHART 19: COMPARING THE INCIDENCE OF MUCINOUS TUMORS IN RELATION TO OTHER STUDIES**

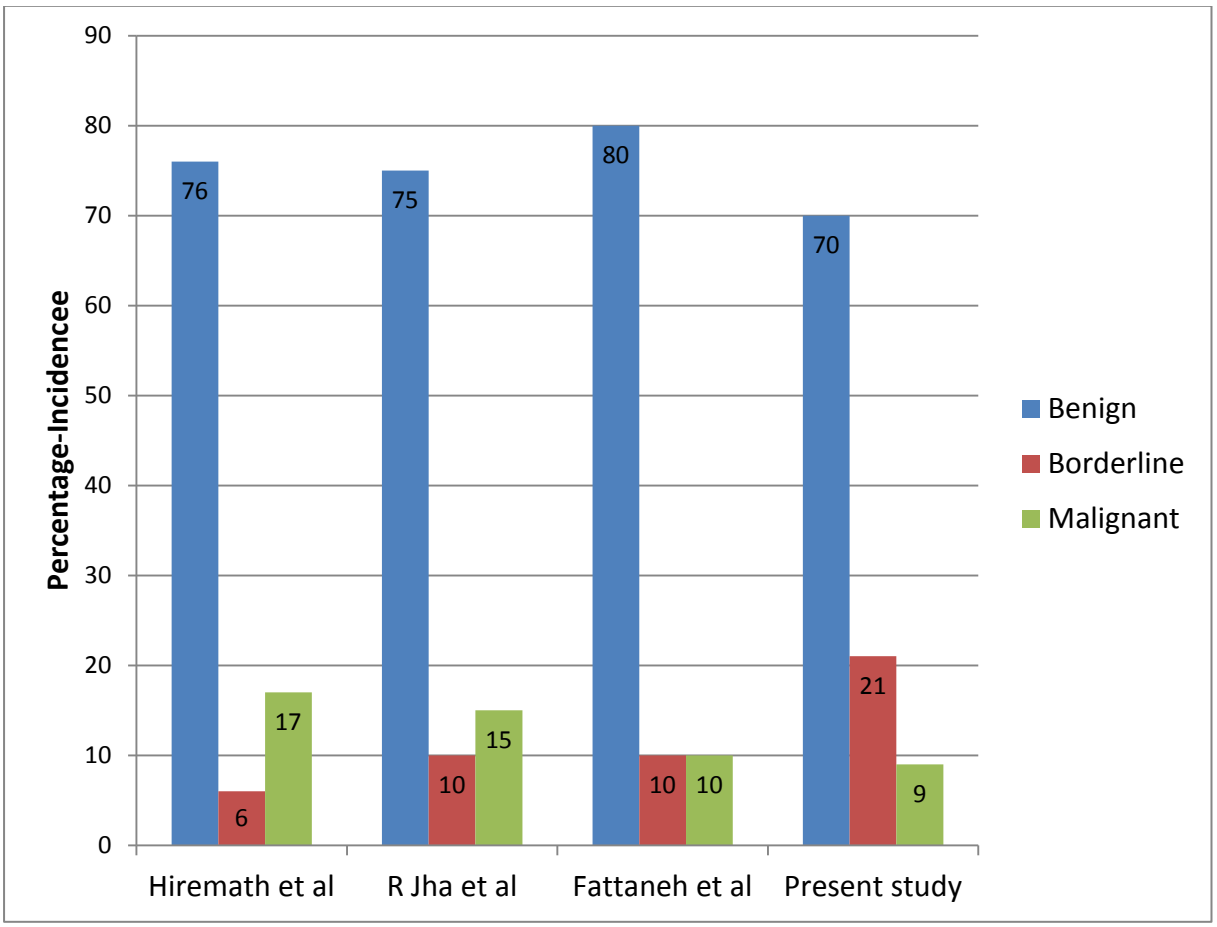


**TABLE 27 : INCIDENCE OF MUCINOUS TUMORS IN RELATION TO OTHER STUDIES:**

| Author | Place of study | Benign | Borderline | Malignant |
|---|---|---|---|---|
| Hiremath et al | Pondicherry | 76% | 6.5% | 17.5% |
| R Jha et al | Nepal | 75% | 10% | 15% |
| Fattaneh et al | India | 80% | 10% | 10% |
| Present study | Thanjavur | 70% | 21% | 9% |

There are about 3 benign Brenner tumors in this study accounting for 3% of all benign surface epithelial tumors. This is in accordance with the journals and literature[16]

Brenner tumors are often associated with other tumors such as ucinous cystadenoma and mature cystic teratoma[44,33]. Inthis study one suchassociation of Brenner tumor with mucinous cystadenoma was found. According to Tsunehisa kaku et al presence of endometriosis is associated with high incidence of ovarian carcinomas , particularly endometrioid carcinoma, clear cell carcinoma, mucinous and serous carcinomas[102,41]. In contrast none of the ovarian tumors in this study was found to be associated with endometriosis.

In this study there are about 24 cases of germ cell tumors, accounting for 16% of all ovarian tumors. Among germ cell tumor group, mature cysticteratoma was the commonest accounting for 91.6%,followed by

dysgerminoma,4.1% and mixed germ cell tumor, 4.1%.This is in accordancewith the study conducted by Fred ureland et al [15]and Kwok et al[46].

According to P.Singh et al [90], age at presentation for malignant transformation in dermoid cyst is older than those with benign disease and is more common in postmenopausal age group. In contrast there were three cases in postmenopausal age group in our study but none of them showed malignant transformation.

According to P.singh et al [90] and Gary et al[19] , Dermoid cysts were the commonest ovarian tumor associated with pregnancy . Similarly in our study , common tumor associated with pregnancy was dermoid cyst, followed by benign mucinous cystadenoma. One case of dysgerminoma and 1 case of mixed germ cell tumor with combination of dysgerminoma and yolk sac tumor component was observed in ourstudy.

In this study, a total of 13 cases, of sex cord stromal tumor accountingfor 8.6% of all ovarian tumors was observed. Of which granulosa cell tumor was the most common type with 9 cases(69%),followed by fibroma with 3 cases(23%),followed by fibrothecoma 1 case,(8%). This finding in our study well correlates with thestudy conducted by R Jha et al[78]

According to Lawrence et al[49] more than 95% of adult granulosa cell tumors are unilateral. Similarly in this study 9/9 cases were unilateral at the time of presentation .According to Fattaneh et al[16] granulosa cell tumors can be associated with endometrial neoplasia. However in this study, none of the 9 cases had any association with endometrial neoplasia.

According to Sung-Jong et al [98], metastatic tumors to the ovaryaccounts for about 5-10% of all ovarian neoplasms. General features of ovarian metastases include bilaterality, surface involvement, extensive extraovarian spread , vascular invasion, desmoplastic reaction & unusual clinical history[45,54].

According to masaki mandai et al[59] , Krukenberg tumor is the most common form of ovarian metastatic carcinoma, often found in the 4$^{th}$decade. It is applied to a clinicopathological entity characterised by presence of mucin – filled , signet ring tumor cells within cellular stroma[59]. In this study, 3 cases ofkrukenberg tumor and one case of metastatic adenocarcinomatous deposits in one ovary of intestinal origin was observed.

In this study p53 immunohistochemical staining of serous carcinomas was done after classifying them as low grade and high grade based on recent 2 tier grading system[3]. Of the 4 low grade serous tumors ,3 (75%) of them stained negatively for p53 . Of the six high grade serous tumors, 5 (90%) of them showed positivity for p53. Of the 4 cases of mucinous carcinoma, al

showed negativity for p53. This finding in our study is well correlated with the studies conducted by Russell Vang et al[80] and Gad Singer etal[17].

Understanding the pathogenesis of Type I and Type II tumors providesclues for new approaches to early detection and treatment[48].

According to Russel pury et al and Scotters et al , although discrepancies exist , epithelial ovarian malignancies showing p53 aberrations are significantly less sensitive to platinum based chemotheraphy and more aggressive than those with functional p53 and hence overexpression of p53 isa poor prognostic factor[52,79].

Tumors of borderline category tends to occur in younger women, often less than 40 yrs of age. Role of conservative surgery may be considered in patients who desire to preserve fertility. However these patients has to becarefully followed up with routine pelvic examinations, serial CA-125 serum levels, ultrasound examination.

According to Steven G. Silverberg et al[95] borderline tumors constitute a unique group characterised by an unusual degree of epithelial cell proliferation and atypia when compared with benign neoplasms. But these borderline tumors lacks stromal invasion which is the characteristic feature ofinvasive tumors[95].

The clinical course of these borderline tumors is in between benign and malignant; they are known to metastasize within the peritoneal cavity but rarely results in death[65].

According to Shappel et al [87], in particular Mucinous borderline tumors, due to the gross and microscopic multiloculation , the identification of stromalinvasion is inherently more difficult . Although several studies including Terilowski et al [100] suggest that the presence of markedly atypical nuclei andstratification to a degree greater than three should prompt the diagnosis ofwell differentiated mucinous carcinoma, even in the absence of frank stromalinvasion[100].

According to Veronique et al[104] morphological changes in the nuclei ofneoplastic cells and their proliferative activity are a significant element ofhistopathlogical examination. In many cases, traditional techniques cannotdefine precisely grading of malignancy, the best evidence of which is tumorsof borderline category[81].

According to Swang maxy[99] et al , proliferative activity of malignant tumors are usually higher than benign and borderline tumors.Determination of proliferative activity of tumors by ki-67 labeliing indexthrough the analysis of MIB-1 monoclonalantibody reactivity will help indifferentiating borderline and malignant tumors.

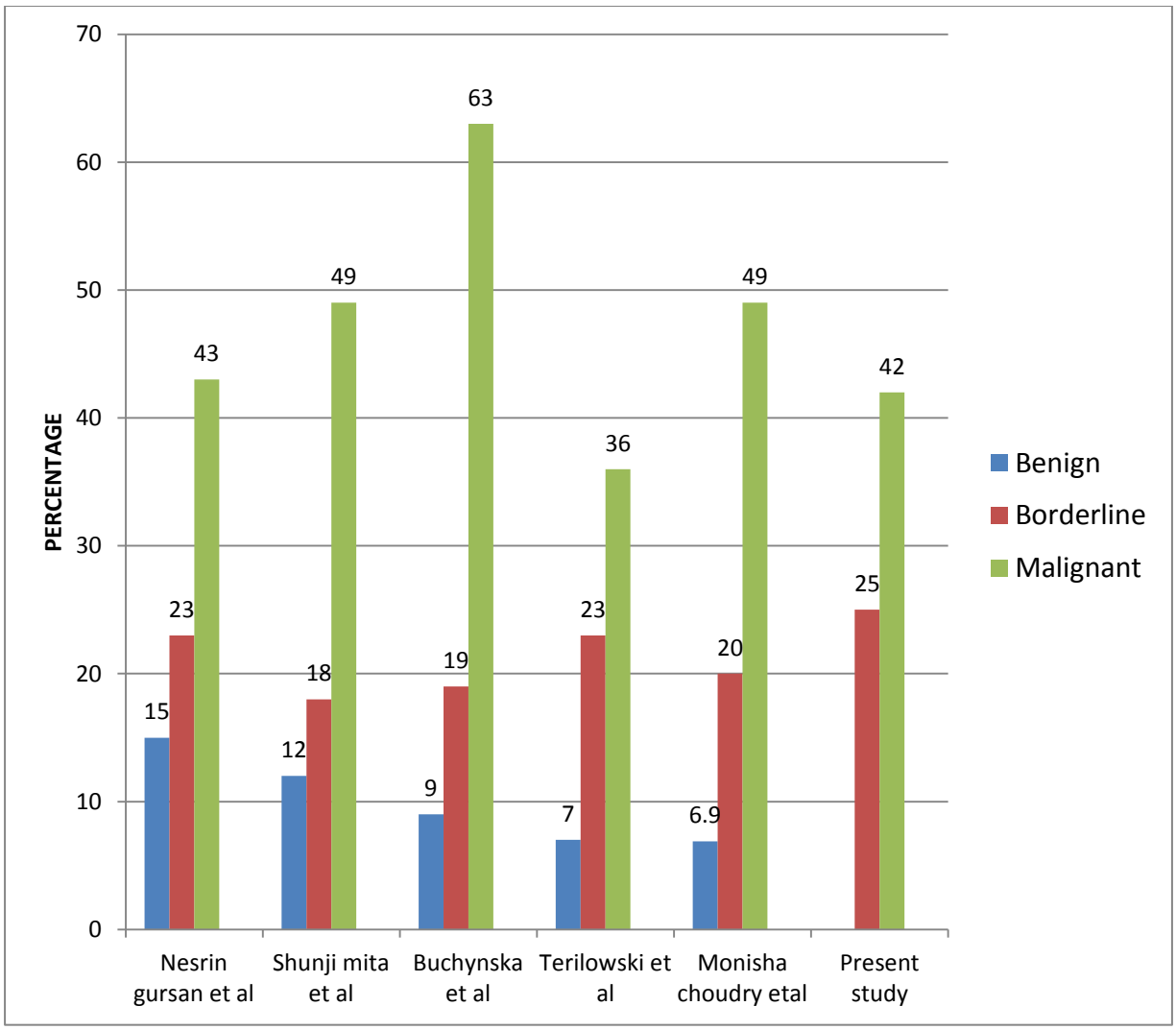
According to GuroAune et al and Henzen et al, patients with ovarian tumors demonstrate potential usefulness of ki-67 antigen expression and its role in predicting the outcome in ovarian cancer. According to Henzen et al ,Terilowski et al and Nesrin gursan et al , malignant epithelial neoplasm had astatiscally significant higher mean ki-67 expression than borderline tumors[34,66,100]. Following table 28 , compares the ki-67 labelling index in epithelial ovarian tumors in this study and various other studies.

**TABLE 28 : COMPARISON OF KI-67 LI IN EPITHELIAL OVARIAN TUMORS WITH OTHER STUDIES:**

| AUTHOR | PLACE OF STUDY | BENIGN | BORDERLINE | MALIGNANT |
|---|---|---|---|---|
| Nesrin gursan et al | Turkey | 14.9% | 22.8% | 42.8% |
| Shunji mita et al | Japan | 12.3% | 21.3% | 48.9% |
| Monisha choudry et al | India | 6.9% | 18% | 49% |
| Terilowsky et al | Poland | - | 23% | 36% |
| Buchynska et al | Ukraine | 8.9% | 21% | 63% |
| Present study | Thanjavur | - | 25% | 42% |

In this study , mean ki-67 expression of malignant epithelial tumors was 42% when compared to borderline tumors with a mean ki-67 LI of 25% and this difference was found to be statistically significant. Statistical analysis was carried out using Students t –test.Shunji mita et al[89], had demonstrated

**CHART 20: COMPARING Ki-67 LABELLING INDEX IN EPITHELIAL OVARIAN TUMORS IN RELATION TO OTHER STUDIES**



Significant relationship between ki-67 antigen expression and long term survival and its role in predicting patients outcome in surface epithelial tumors[89].

Although the staining pattern for ki-67 in predicting malignant versus borderline tumors is statistically significant, they are applied only in difficult cases[55]. According to Lobna ayadi et al and Mary T Sylvia et al , more importantly a panel of markers like p53, bcl-2 and ki-67 , all of which reflectsthe proliferative activity of the tumor should be used and it may further definethe biologic potential of a specific tumor[{66,55,57}.]

# CONCLUSION

# CONCLUSION

In our study a total of 150 cases were evaluated with clinical , histopathological & immunohistochemistry and the following conclusions were made and presented.

1. The incidence of ovarian neoplasms among all female neoplasms is 7.8%
2. The incidence of ovarian malignancies among all female malignancies is 2.6%
3. Ovarian malignancy ranks 2$^{nd}$ (4.7%) among the female genital tract Malignancies.
4. The ratio of benign and malignant ovarian neoplasm is 3:1
5. The incidence of ovarian neoplasm is highest during the 2$^{nd}$ decade followed by 4$^{th}$ decade.
6. 90% of ovarian neoplasms are unilateral and 10% are bilateral at the time of presentation
7. Benign neoplasms are predominantly cystic, whereas malignant neoplasms are predominantly solid and cystic or purely solid.
8. Surface epithelial tumors are the most common neoplasm of which Serous cysadenoma is the commonest.

9. Detecting p53 mutations by immunohistochemistry in surface epithelial neoplasms helps to understand the pathogenesis of Type I and Type II ovarian neoplasms.

10. Increased expression of Ki-67 LI was found in malignant surface epithelial neoplasms when compared to borderline epithelial neoplasms and it is statistically significant.

This study is an institution based one and has small sample size of 150 cases. So the results obtained may or may not reflect the actual histological pattern and age distribution of ovarian cancer in Indian women. The epidemiological pattern of cancers in developing countries differs in many aspects from developed nations. The age specific incidence of ovarian cancer and its subtypes presented in this study will serve as a useful point of reference for future studies and would help to specify their trend in future and encompass the community health programs to solve health problems.

# APPENDIX

# APPENDIX I

## HAEMATOXYLIN AND EOSIN STAIN

### Preparation of solution :

### HARRIS HAEMATOXYLIN

Distilled water-1000ml

Ammonium alum-100g

Absolute ethyl alcohol-50ml

Mercuric oxide-2.5g

100g of ammonium alum dissolved in 1000ml of distilled water by heating and shaking at 60.c .Add solution of 5g of haematoxylin in 50ml of ethylalcohol and bring rapidly to boil.when it begins to boil,remove from flame and add 2.5 g of mercuric oxide. Mix by swirling gently.

### EOSIN STAIN

Eosin Y- 1 g.

Distilled water-20ml.

95% ethanol-80ml

Glacial acetic acid-0.2ml

Dissolve 1 gm of eosin Y in 20ml of water ,add 80 ml of 95% ethyl alcohol and 0.2 ml of glacial acetic acid.

**Procedure :**

1. Bring the sections to water
2. Dip in Harris haematoxylin for 15 minutes.
3. Rinse in tap water.
4. Differentiate in 1% acid alcohol-3-4 quick dips.
5. Wash in tap water briefly.
6. Dip in ammonia water or saturated lithium carbonate until the sections are blue.
7. Wash in running tap water for 10-20 minutes.
8. Stain with eosin for 15 seconds to 2 minutes depending on the age of the eosin and the depth of counter stain.
9. Rinse in tap water.
10. Dip in 95% alcohol
11. 3 changes in absolute alcohol.
12. Xylene – 2 changes.
13. Mount in DPX mountant.

# APPENDIX II

## IMMUNOHISTOCHEMISTRY

## PREPARATION OF SOLUTIONS:

## Tris buffer saline (TBS): 0.005M

Distillled water-10 litres

Sodium chloride- 80gms

Tris (hydroxymethylamine)-6.05g

1 M Hcl-44 ml.

Final pH is adjusted to 7.6 with either 1 M Hcl or 0.2 M Tris solution.

**CITRATE BUFFER SOLUTION:**

Trisodium citrate-2.94 gm

1 N Hcl-5ml

Distilled water-1000 ml

Final ph is adjusted to 6.0 with 1 N H cl.

**Preparation of gelatine coated slides:**

Chrome alum-0.05gm

Gelatine-0.3 gm

Distilled water-100 ml.

Chrome alum is added to distilled water and then hheated to 60.c.gelatin is added slowly to the heated distilled water. Glass slides are then dipped in this solution and dried overnight.

**Antigen retrieval:**

The slides are placed in citrate buffer in the coplin jar and capped. The jar is

then heated in a 750 W domestic microwave oven for 15 minutes.

**Procedure :**

1. Dewax the section in xylene(1/2 hr, 2 changes) and bring sections to distilled water.
2. Antigen retrievel using TBS by microwave oven heating
3. Cool to room temperature in running tap water for 20 mintues.
4. Bring the section toTBS for 5 minutes.
5. Drain and wipe off excess TBS around sections
6. Incubate in endogenous peroxidise blocking agent for 15-20 minutes.
7. Gently wash the slide in TBS for 5 minutes.
8. Wipe off excess fluid and incubate in power block for 15-20 minutes
9. Blot and dry excess power block.
10. Incubate in primary antibody for 60 minutes.
11. Repeat steps 4 and 5 .
12. Incubate in superenhancer for 30 minutes.
13. Repeat steps 4 and 5.
14. Incubate in secondary antibody for 30 minutes.
15. Repeat steps 4 and 5
16. Incubate in DAB(DiaminoBenzidine) substrate buffer for 2-10 minutes
17. Wash in distilled water counter stain with haematoxylin,clear in xylene and mount with DPX.

**APPENDIX III**

Tumor, Node, Metastasis(TNM) Staging Scheme for ovarian carcinomas:

PRIMARY TUMOR (T)

TNM Category International Federation of Gynaecology and Obstetrics-FIGO

TX Primary tumor cannot be assessed

T0 No evidence of primary tumor

T1 I Tumor limited to ovaries(one or both)

T1a 1A Tumor limited to one ovary; capsule intact, no tumor on surface or no malignant cells in ascites/ peritoneal washings.

T1b IB Tumor limited to both ovaries, capsule intact, no tumor on surface or no malignant cells in ascites/ peritoneal washings.

T1c IC Tumor limited to one or both ovaries with any of the following: capsule ruptured, tumor on ovarian surface, malignant cells in ascites or peritoneal washings.

T2 II Tumor involves one or both ovaries with pelvic extension and/or implants

T2a IIA Extension and/or implants on uterus and /or tubes. No malignant cells in ascites or peritoneal washings

T2b IIB Extension to and/or peritoneal implants to other pelvic tissues. No malignat cells in ascites or peritoneal washings.

T2c II C Pelvic extension and/or implants with malignant cells in peritoneal washings or ascites.

T3 and/or N1 III Tumor involves one or both ovaries with microscopically confirmed peritoneal metastasis outside the pelvis.

T3a IIIA Microscopic peritoneal metastasis beyond the pelvis (no macroscopic tumor).

T3b III B Macroscopic peritoneal metastasis beyond the pelvis < 2 cm

in greatest dimension.

T3c III C Macroscopic peritoneal metastasis beyond the pelvis > 2 cm

in greatest dimension.

M1 IV Distant metastasis (excludes peritoneal metastasis)

REGIONAL LYMPHNODE (N):

NX Regional lymph nodes cannot be assessed

N0 No regional lymphnode metastasis.

N1 Regional lymphnode metastasis.

DISTANT METASTASIS(M):

MX Distant metastasis cannot be assessed

M0 No distant metastasis.

M1 Distant metastasis (excludes peritoneal metastasis).

STAGE GROUPING:

Stage IA: T1a N0 M0

Stage 1B: T1b N0 M0

Stage 1C: T1c N0 M0

Stage IIA: T2a N0 M0

Stage IIB: T2b N0 M0

Stage IIC: T2c N0M0

Stage IIIA: T3a N0 M0

Stage IIIB: T3b N0 M0

Stage IIIC: T3c N0 M0

Any T N1 M0

Stage IV : Any T Any N M1.

# BIBLIOGRAPHY

# BIBLIOGRAPHY


1. Adhikari et al . Granulosa cell tumor of the ovary: a clinicopathological study of six cases. Journal of pathology of Nepal (2011) vol.1 96-99.

2.Adriana Dionigi et al .ovarian metastases from colorectal carcinoma. American journal of clinical pathology 2000,114, page no.111-122

3. Anais malpaica et al .Grading of ovarian serous carcinoma using two-tier grading system.American journal of surgical pathology .vol28 Number 4 April 2004.

4. Aparna rajesh et al .Fibroma of ovary presenting as meigs syndrome. A case report –NUJHS vol 2 no.3,sep.2012.

5.Balkrishna bhika yeole et al .An assessment of cancer incidence patterns in parsi and non parsi populations, Mumbai.Asian pacific journal of cancer prevention ,vol2,2001.

6.Brigette M.Ronnett et al.Mucinous borderline ovarian tumors: points of general aggrement and persisteny controversies.Journal of human pathology 2004 446-458.

7.Buchynska.L.G. et al.Expression of P53,P21,P16,KI-67 proteins in serous ovarian tumors.Experimental oncology 2007 vol29.49-53.

8.Burger PC etal .the use of monoclonal antibody ki-67 antigen in the identification of proliferating cells. Am.J.Surg pathology 1986; 10:611-617.

9.Buttitta .F et al .P53 alterations are predictive of chemoresistance and aggressiveness in ovarian carcinoma:a molecular and immunohistochemical study.British journal of cancer 1997.vol75,230-235.

10 .Cecile le page et al. Predictive and prognostic biomarkers in epithelial ovarian cancer:recommendation for future studies. Cancers 2010,2,913-954.

11 .Charitini komodiki et al . ovarian cancer .MECC monograph. 2006.vol 1 26-28.

12.Dar etal. Clinical and pathological study of ovarian serous borderline tumors.cancer research on 17-08-2011.

13.Debra A. Bell et al .serous borderline (low malignant potential,atypaical proliferative) ovarian tumors: workshop perspectives.Journal of human pathology 2004 (35)934-938 .
14. Ferlay et al .risk factors and age distribution in Ireland.1995-2007.
15. Fred ueland et al .Germ cell and stromal cell tumors of ovary.2008; vol 24:323-326.
16.Fattaneh .A.Tavassoli et al .WHO classification of tumors-pathology and genetics-tumors of breast and female genital tract system.IARC Press Lyon 2003.
17.Gad singer et al .patterns of p53 mutations separate ovarian serous borderline tumors ansd low grade and high grade serous carcinomas and provide support for a new model of ovarian carcinogenesis.Am.J.surg.pathilogy2005,vol29,no.2,feb,218-224.
18.G.Gangadar swamy et al. Clinicopathological analysis of ovarian tumors- a study on five years sample.Nepal med coll J.2010,vol12,221-223.
19. Gary s leiserowitz et al .Management of ovarian masses during pregnancy. Journal of Obstetrics and gynaecological surgery.2006 vol6,no.7.
20. Geunghwan Ahn,et al .An update on ovarian surface epithelial tumors of ovary.
21.Geza Acs,et al. Serous and mucinous borderline tumors of ovary.AM J Clin.Pathology 2005, 123.
22.Gioele G etal: ki-67 antigen immunostaining in serous ovarian tumors ; index of proliferative activity with prognostic significance. International journal of gynaecology oncology 1995;56;169-174.
23.Giuseppina et al. Epithelial ovarian carcinoma: the role of cell cycle genes in the different histotypes. Open clinical research cancer journal 2008, 2, 7-12.
24.Glenn Mc cuggage et al .Morphological subtype of ovarian Carcinoma,a review with emphasis on new develop and pathogenesis,pathology august 2011 vol 43.page no.420-432.
25. Goitem hagos et al .Meigs syndrome: a case report and literature review .journal of eriterean medical association (JEMA).2009.

26. Gozde kir et al .Clinicopathological and immunohistochemical profile of ovarian metastases from colorectal carcinoma. World journal of gastrointestinal surgery 2010. April 27,109-116.
27.Guro Aune et al; the proliferation markers ki-67, survivin may contribute to the identification of aggressive ovarian carcinomas. International journal of clinical exp. Pathology 2011;4(5): 444-453.
28. Halperin.R. et al. Clinical and molecular comparison between borderline serous ovarian tumors and advanced serous papillary ovarian carcinoma. European journal of gynaecologic oncology 2001 ,22(4),292-296.
29.Hampton et al. Gene expression profiles in serous borderline tuomrs,low grade serous carcinoma and high grade serous carcinoma, 2005 vol. 24: 1053.
30. Hasson E.et .al. ovarian tumors during childhood and adolescence. A clincopathological study European journal of Gyneacological oncology 1999,20:124-126.
31.Herod JO et al. The prognostic significance of bcl-2 and p53 expression in ovarian carcinoma. Cancer research 1996;56:2 178-184.
32. Hiremath . P.B et al .clinical profile and pathology of ovarian tumor .International journal of biological and medical research.2012 ,3 :1743-1746.
33.Heye et al. Left ovarian Brenner ovarian tumor JBR-BTR 2005 vol88(5).page no 245-247.
34. Henzen S .C –Lognnans et al .Ki-67 staining in benign,borderline,malignant primary and metastatic ovarian tumors. Correlation with steroid receptors/EGFR/CathepsinD. International journal of cancer 1994 may 15 page no-468-472.
35.Hitchcock CL etal: ki-67 staining as a means to simplify analysis of tumor cell proliferation. American Journal of clinical pathology 1991; 96:444-446.
36. Iavazzoc et al.Meigs/pseudomeigs syndrome.case report.bratisl Lee Listy 2007,108(3) 158-160.
37. Inderbir singh et al. Human embryology .seventh edition .2008
38. In Ho Lee et al .Clinicopathological characteristics of granulose cell tumors of the ovary:multicentre retrospective study.

39. Irfan cicin et al. Yolk sac tumors of ovary.evaluation of clinicopathological features and prognostic factors..European journal of obstetrics and gynaecology.february 2009.
40. Irving et al . Cellular fibroma of ovary : A study of 75 cases including mitotically active fibroma. American journal of surgical pathology 2006, August 30 (8) 929-938..
41. Jaime et al .Clinicopathological characteristics of ovarian carcinoma associated with endometriosis. Archieves of Gynaecology and Obstetrics. 2011 vol28,no.2 page no.479-483.
42. Jeffrey.T.Quirk et al .risk factors for invasive epithelial ovarian carcinoma by histological subtype.2004,vol3.
43. Jeffrey.D.Seidman et al .borderline ovarian tumors: Diverse contemporary view points on terminology and diagnostic criteria.
44. Jeffray SD Russell P ,Robert KJ. Surface epithelial tumors .In Robert kurman J. Blausteins pathology of female genital tract,fifth edition.2002:791-881.
45. Juan RI, Rosai and Ackermans surgical pathology. tenth edition 2011 Kondipaffiti et al.
46. KKM Kwok et al. Malignant mixed germ cell tumor of ovary in a 10yr old girl.JHK Coll Radiology 2008;11;92-95.
47. Kwan ghee kim et al.Bilateral ovarian carcinoma metastases from the ampulla of vater: a rare krukenberg tumor.Journal of Korean Med.science.1999,vol 14,220-222.
48. Kurman R.J. et al . Molecular pathogenesis and extra ovarian origin of epithelial ovarian cancer shifts the paradigm. Human pathology 2011vol 42,918-931.
49. Lawrence M.Roth et al . Recent advances in the pathology and classification of ovarian sex cord-stromal tumors.International journal of gynaecological pathology2006 vol25,199-215.
50. Lee C H et al.Torsion of ovarian tumors : a clinicopathological study.International Journal of Gynaecology and obstetrics 1989 vol28,page no.21-25.
51. Lee.G.et al.Fine needle aspiration cytology in the diagnosis and classification of recurrent and metastatic gynaecological malignancies.1988.vol29,375-378.

52. Lee.H.et al Diagnostic approach using the expression profiling p53 tumor suppressor gene and its related proteins in ovarian epithelial tumors.Int.J. of Gynaecological cancer 2005, 15(3):453-461.
53. Lee .KR.et al .The distinction between primary and metastatic mucinous carcinomas of ovary: gross and histologic findings in 50 cases. American Journal of surgical pathology 2003 ;27 : 281-292.
54. Lash RH et al. Intestinal adenocarcinomas metastatic to ovaries..A Clinicopathological evaluation of 22 cases. American journal of surgical pathology 1987;11: 114-121.
55. Lobna Ayadi et al.Correlation between immunohistochemical biomarkers expression and prognosis of ovarian carcinomas in tunision patients.World journal of oncology.Vol.1.no.3.jun.2010 118-128.
56. Malieh Arab at al.Crude and age incidence rate patterns for histopathologic subtypes of ovarian cancer in iran.Archieves of Iranian medicine 2010 vol 13,no.3,may 2010
57. Mary T Syllvia et al.the expression of immunohistochemical markers ER,PR,P53,KI-67,HER2neu in epithelial ovarian tumors and its correlation with clinical variables.Indian Journal of Pathology and Microbiology.2012 vol55.page.33-37.
58. Manoharan.N.et al.Cancer incidenes in Urban delhi-2001-2005.Asian pacific journal of cancer prevention 2009,vol10.
59. Masaki Mandai et al . Krukenberg tumors .CME Journal of Gynaecologic oncology,2004,vol 9,112-114.
60. Monisha choudhry et al .A cytohistological study of ki-67 expreession of ovarian tumors.Indian journal of pathology and microbiology .2011 .vol54, page21-24.
61. Migraci tosun et al . Adnexal masses in pregnancy-a series of 12cases. Perinatal journal 2010 ,vol18 ,issue 2.
62. Min jae kim et al .clinical characteristics of ovarian teratoma-American journal of obstetrics and gynaecology-2011;205:32.
63. Nancy Hamel et al.Mixed ovarian germ cell tumor in a BRCA2 gene mutation carcinoma.International journal of gynaecological pathology2007,vol 26, page no.160-164

64. Nandagudi srinivasa murty et al . Changing trend in incidence of ovarian cancer-the Indian scenario.Asian pacific journal of cancer prevention vol 10 2009.
65. Neeraj Lalwani et al.Current update on borderline ovarian tumors.AJR: 194,Feb 2010. 330-335.
66. Nesrin gursan et al .P53 ,Bcl-2,ki-67,status in benign borderline,malignant ovarian surface epithelial neoplasms. Eurasian journal of medicine .april 2009,vol41.
67. Niwa K et al. Alteration of p53 gene in ovarian carcinoma ; clinicopathological correlation and prognostic significance. British journal of cancer 1994; 70: 1191-7.
68. Pilli GS et al Ovarian tumors : a study of 282 cases. Journal of Indian medical association 2002,100; 420, 423-424.
69. Population based cancer registry,Bangalore, Kidwai memorial institute of oncology, Bangalore HBCR :2001-2003.
70. Population based cancer registry, Bhopal-Gandhi medical college, HBCR: 2001-2003.
71. Population based cancer registry, Chennai-cancer institute(WIA) adayar,Chennai.HBCR: 2001-2003.
72. Rajaraman Swaminathan et al the international journal of cancer epidemiology,detection and prevention.2009.vol33,325-331.
73. Ramzy et al.Early surface epithelial tumors of ovary-Diagnostic challenges and controversies-University of California Irvine 2004.
74. Rashid et al. A. Clinicopathological study of ovarian cancer international journal of clinical pathology 1998; 36:117-125.
75. Robert A.soslow .histological subtypes of ovarian carcinoma:an overview.the international journal of gynaecological pathology 2008 .vol27,161-174.
76.Robert J.Kurman .Blausteins pathology of female genital tract 5th edition page no.758-768.
77. Rodriguez et al . Mucinous tumors of ovary: clinicopathological analysis of borderline ovarian tumors. American journal of surgical pathology 2002, feb 26 (2) 139-152.
78. Runa jha et al.Histological pattern of ovarian tumors and their age distribution .Nepal medical college journal 2008; vol10 ,81-85.

79.Russel Petty et al .Drug resistance in ovarian cancer-the role of p53.pathology oncology research,vol 4,no.2,1998.
80. Russel vang et al.Ovarian low-grade and high grade serous carcinoma: pathogenesis ,clinicopathological and molecular biologic features, diagnostic problems . Adv .anat .pathology 2009 , vol16,267-282.
81. Rutgers JL et al . Ovarian mixed –epithelial papillary cystadenomas of borderline malignancy of mullerian type. A clincopathological analysis .Cancer journal 1988; 61: 340-348.
82.Saadia tariq et al .study of ovarian tumors in young girls.professional med.journal 2011,vol18,41-45.
83. Samina Zaman et al. A retrospective study of ovarian tumors and tumor like lesions . Journal Ayub Med Coll Abottabad2010 vol 22.
84. Sarah saheed et al.Epithelial ovarian cancer; epidemiology and clinicopathological features.professional Med journal 2012 vol19,40-45.
85. Sah SP et al .Germ cell tumors of the ovary; A clinicopathological study of 121 cases . Journal Obsetrics and Gynaecology Resi 2004;30: 303-308.
86. Shahbaz sarwar et al. Epithelial ovarian cancerat a cancer hospital in a developing country.Asian pacific cancer journal of cancer prevention.2006 vol7.
87. Shappel et al.Diagnostic criteria and behaviour of ovarian seromucinous tumors: American journal of surgical pathology 2002; 26: 1529-41.
88. Shruti shah et al.Incidence and management of ovarian tumors .Bombay hospital journal 2008 vol50 no.1.
89.Shunji mita et al.Prognostic significance of Ki-67 antigen immnuostaining in ovarian cancer.journal Nippon med sch 2004,vol71(6).
90. Singh et al .Malignancy associated with benign cystic teratomas of the ovary.Sing.Med journal 1988,vol29,30-34.
91.Soetters.R.P et al. Aspects of early epithelial ovarian cancer.Menopause update vol 12,no.1,February 2009.
92. Stacey .E.Mills .Sternbergs Diagnostic surgical pathology vol II 5th edition.

93. Stanley .J..Robbins – Robboys pathology of female genital tract.2nd edition.
94. Steven .G.Silverberg. Principles and practice of of surgical pathology and cytopathology.Fourth edition vol 2.
95. Steven G. Silverberg et al.Borderline ovarian tumors;key points and workshop summary. journal of human pathology 2004.page no.910-916.
96. Sujatha pudasaini et al .A study of ovarian neoplasma in a tertiary hospital of Kathmandu valley.Nepal Med coll Journal 2011,vol13,page no. 39-41.
97. Sumaira yasmin et al .Clinicopathological patterns of ovarian tumors in Peshawar region.Journal Ayub.med.coll Abottabad,2008,vol20(4).
98. Sung –Jong Lee et al. Clinical characteristics of metastatic tumors to ovaries. Journal Korean med science 2009,24,114-119.
99. Swang Maxy et al .Expression of ki-67,PCNA& Mitotic index in epithelial ovarian tumors.Journal of Sichuan university; medical science edition : 2010 vol 12.
100. Terilowski et al.Study of borderline and invasive mucinous ovarian tumors using Ki-67( MIB-1) antibodies and nucleolar organiser region staining.Arch.gynaecology and obstetrics 1999,263: 29-33.
101. Terzaki's et al .Proliferating Brenner tumor of ovary.clinicopathological analysis of 2 cases and review of literature. Eurasian journal of Gynaecological oncology 2011 vol 32 (5)
102. Tsunehisa kaku et al. Histological classification of ovarian carcinoma. Med.Electron Microscopy. 2003 . vol36: 9-17.
103. Viale G et al .the combined evaluation of p53 accumulation and of ki-67 labelling index provides independent information on overall survival of ovarian carcinoma. Anals of oncology 1997; 8: 469-476.
104. Veronique ouellet et al .Immunohistochemical profiling of benign,borderline,low grade malignant serous epithelial tumors.BMC Cancer-2008,8: 346.
105. Vivien .W.Chen et al .Pathology and classification of ovarian tumors. supplement to Cancer-North American association of central cancer registries.2003,January 15.

106. Yasmin Bhurgri et al .Incidence,trends and morphology of ovarian cancer in Karachi(1995-2002). Asian pacific journal of cancer prevention vol12, 1567-1571.